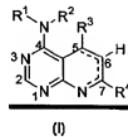




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(54) Title: 5,7-DISUBSTITUTED-4-AMINOPYRIDO[2,3-D]PYRIMIDINE COMPOUNDS



(57) Abstract

A method of inhibiting adenosine kinase by administering one or more compounds of formula (I), wherein R¹, R², R³ and R⁴ are defined, a pharmaceutical composition comprising a therapeutically effective amount of a compound thereof above in combination with a pharmaceutically acceptable carrier, and a method of treating cerebral ischemia, epilepsy, nociception, inflammation and sepsis in a mammal in need of such treatment, comprising administering to the mammal a therapeutically effective amount of a compound thereof, a process for preparing said compounds, and compounds having the above formula wherein R¹, R², R³ and R⁴ are separately defined.

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5,7-DISUBSTITUTED-4-AMINOPYRIDO[2,3-D]PYRIMIDINE COMPOUNDS

This application is a continuation in part of copending U.S. Patent Application Serial No. 09/176,521 filed October 21, 1998 which in turn is a continuation in part of copending U.S. Patent Application Serial No. 09/062,796 filed April 13, 1998, which in turn is a conversion of Provisional U.S. Patent Application Serial No. 60/043,251, filed 5 April 16, 1997.

TECHNICAL FIELD

The present invention relates to a method of inhibiting adenosine kinase by administering 5,7-disubstituted-4-aminopyrido[2,3-d]pyrimidine compounds to a mammal 10 in need of such treatment, to pharmaceutical compositions containing such compounds, as well as to certain 5,7-disubstituted-4-aminopyrido[2,3-d]pyrimidine compounds.

BACKGROUND OF THE INVENTION

Adenosine kinase (ATP:adenosine 5'-phosphotransferase, EC 2.7.1.20) is a 15 ubiquitous enzyme which catalyzes the phosphorylation of adenosine to adenosine monophosphate (AMP), using adenosine triphosphate (ATP), preferentially, as the phosphate source. Magnesium is also required for the reaction, and the true cosubstrate is probably the MgATP²⁻ complex (Palella, et al., *J. Biol. Chem.* 1980, 255: 5264-5269). Adenosine kinase has been isolated from yeast (Leibach, et al., *Hoppe-Seyler's Z. Physiol. Chem.* 1971, 352: 328-344), a variety of mammalian sources (e.g. Miller, et al., *J. Biol. Chem.* 1979, 254: 2339-2345; Palella, et al., *J. Biol. Chem.* 1980, 255: 5264-5269; Yamada, et al., *Comp. Biochem. Physiol.* 1982, 71B: 367-372; Rottlan and Miras-Portugal, *Eur. J. Biochem.*, 1985, 151: 365-371), and certain microorganisms (e.g. Lobelle-Rich and Reeves, *Am. J. Trop. Med. Hyg.* 1983, 32: 976-979; Datta, et al., *J. Biol. Chem.* 1987, 262: 5515-5521). It has been found to be present in virtually every human 20 tissue assayed including kidney, liver, brain, spleen, placenta and pancreas (Andres and Fox, *J. Biol. Chem.* 1979, 254: 11388-11393).

Adenosine kinase is a key enzyme in the control of intracellular adenosine concentration (Arch and Newsholme, Essays Biochem. 1978, 14: 82-123). Adenosine is a purine nucleoside that is an intermediate in the purine nucleotide degradation and salvage. Adenosine also has many important physiologic effects, many of which are mediated 5 through the activation of specific ectocellular receptors, termed P1 receptors (Burnstock, in Cell Membrane Receptors for Drugs and Hormones, 1978, (Bolis and Straub, eds.) Raven, New York, pp. 107-118; Fredholm, et al., Pharmacol. Rev. 1994, 46: 143-156).

In the central nervous system, adenosine inhibits the release of certain neurotransmitters (Corradetti, et al., Eur. J. Pharmacol. 1984, 104: 19-26), stabilizes 10 membrane potential (Rudolphi, et al., Cerebrovasc. Brain Metab. Rev. 1992, 4: 346-360), functions as an endogenous anticonvulsant (Dragunow, Trends Pharmacol. Sci. 1986, 7: 128-130) and may have a role as an endogenous neuroprotective agent (Rudolphi, et al., Trends Pharmacol. Sci., 1992, 13: 439-445). Adenosine may play a role in several 15 disorders of the central nervous system such as schizophrenia, anxiety, depression and Parkinson's disease (Williams, M., in Psychopharmacology: The Fourth Generation of Progress, Bloom, Kupfer (eds.), Raven Press, New York, 1995, pp 643-655. Adenosine has also been implicated in modulating transmission in pain pathways in the spinal cord (Sawynok, et al., Br. J. Pharmacol., 1986, 88: 923-930), and in mediating the analgesic 20 effects of morphine (Sweeney, et al., J. Pharmacol. Exp. Ther. 1987, 243: 657-665). Adenosine also, inhibits certain neutrophil functions and exhibits anti-inflammatory effects (Cronstein, J. Appl. Physiol. 1994, 76: 5-13). An AK inhibitor has been reported to decrease paw swelling in a model of adjuvant arthritis in rats (Firestein, et.al., Arthritis and Rheumatism, 1993, 36, S48.

Adenosine also exerts a variety of effects on the cardiovascular system, including 25 vasodilation, impairment of atrioventricular conduction and endogenous cardioprotection in myocardial ischemia and reperfusion (Mullane and Williams, in Adenosine and Adenosine Receptors, 1990 (Williams, ed.) Humana Press, New Jersey, pp. 289-334). The widespread actions of adenosine also include effects on the renal, respiratory, gastrointestinal and reproductive systems, as well as on blood cells and adipocytes.

Adenosine, via its A₁ receptor activation on adipocytes, plays a role in diabetes by inhibiting lipolysis (Londos, et al., *Proc. Natl. Acad. Sci.* USA, 1980, 77, 2551).

Endogenous adenosine release appears to have a role as a natural defense mechanism in various pathophysiologic conditions, including cerebral and myocardial 5 ischemia, seizures, pain, inflammation and sepsis. While adenosine is normally present at low levels in the extracellular space, its release is locally enhanced at the site(s) of excessive cellular activity, trauma or metabolic stress. Once in the extracellular space, adenosine activates specific extracellular receptors to elicit a variety of responses which tend to restore cellular function towards normal (Bruns, *Nucleosides Nucleotides*, 1991, 10: 931-943; Miller and Hsu, *J. Neurotrauma*, 1992, 9: S563-S577). Adenosine has a half-life measured in seconds in extracellular fluids (Moser, et al., *Am. J. Physiol.* 1989, 25: C799-C806), and its endogenous actions are therefore highly localized.

The inhibition of adenosine kinase can result in augmentation of the local 15 adenosine concentrations at foci of tissue injury, further enhancing cytoprotection. This effect is likely to be most pronounced at tissue sites where trauma results in increased adenosine production, thereby minimizing systemic toxicities.

Pharmacologic compounds directed towards adenosine kinase inhibition provide 20 potentially effective new therapies for disorders benefited by the site- and event-specific potentiation of adenosine. Disorders where such compounds may be useful include ischemic conditions such as cerebral ischemia, myocardial ischemia, angina, coronary artery bypass graft surgery (CABG), percutaneous transluminal angioplasty (PTCA), stroke, other thrombotic and embolic conditions, and neurological disorders such as epilepsy, anxiety, schizophrenia, nociception including pain perception, neuropathic pain, visceral pain, as well as inflammation, arthritis, immunosuppression, sepsis, diabetes 25 and gastrointestinal dysfunctions such as abnormal gastrointestinal motility.

A number of compounds have been reported to inhibit adenosine kinase. The most potent of these include 5'-amino-5'-deoxyadenosine (Miller, et al., *J. Biol. Chem.* 1979, 254: 2339-2345), 5-iodotubercidin (Wotring and Townsend, *Cancer Res.* 1979, 39: 3018-3023) and 5'-deoxy-5-iodotubercidin (Davies, et al., *Biochem. Pharmacol.* 1984, 33: 347-355).

Adenosine kinase is also responsible for the activation of many pharmacologically active nucleosides (Miller, et al., J. Biol. Chem., 1979, 254: 2339-2345), including tubercidin, formycin, ribavirin, pyrazofurin and 6-(methylmercapto)purine riboside. These purine nucleoside analogs represent an important group of antimetabolites which possess 5 cytotoxic, anticancer and antiviral properties. They serve as substrates for adenosine kinase and are phosphorylated by the enzyme to generate the active form. The loss of adenosine kinase activity has been implicated as a mechanism of cellular resistance to the pharmacological effects of these nucleoside analogs (c.g. Bennett, et al., Mol. Pharmacol., 1966, 2: 432-443; Caldwell, et al., Can. J. Biochem., 1967, 45: 735-744; Suttle, et al., 10 Europ. J. Cancer, 1981, 17: 43-51). Decreased cellular levels of adenosine kinase have also been associated with resistance to the toxic effects of 2'-deoxyadenosine (Hershfield and Kredich, Proc. Natl. Acad. Sci. USA, 1980, 77: 4292-4296). The accumulation of deoxyadenosine triphosphate (dATP), derived from the phosphorylation of 2'-deoxyadenosine, has been suggested as a toxic mechanism in the immune defect 15 associated with inheritable adenosine deaminase deficiency (Kredich and Hershfield, in The Metabolic Basis of Inherited Diseases, 1989 (Scriven, et al., eds.), McGraw-Hill, New York, pp. 1045-1075).

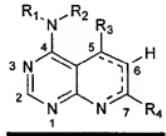
B.S. Hurlbert et al. (J. Med. Chem., 11: 711-717 (1968)) disclose various 2,4-diaminopyrido[2,3-d]pyrimidine compounds having use as antibacterial agents. R. K. 20 Robins et al. (J. Amer. Chem. Soc., 80:3449-3457 (1958)) disclose methods for preparing a number of 2,4-dihydroxy-, 2,4-diamino-, 2-amino-4-hydroxy- and 2-mercaptop-4-hydroxypyrido[2,3-d]pyrimidines having antifollic acid activity. R. Sharma et al., (Indian J. Chem., 31B: 719-720 (1992)) disclose 4-amino-5-(4-chlorophenyl)-7-(4-nitrophenyl)pyrido[2,3-d]pyrimidine and 4-amino-5-(4-methoxyphenyl)-7-(4-nitrophenyl)pyrido[2,3-d]pyrimidine compounds having antibacterial activity. A. Gupta et 25 al., (J. Indian Chem. Soc., 71: 635-636 (1994)) disclose 4-amino-5-(4-fluorophenyl)-7-(4-fluorophenyl)pyrido[2,3-d]pyrimidine and 4-amino-5-(4-chlorophenyl)-7-(4-fluorophenyl)pyrido[2,3-d]pyrimidine compounds having antibacterial activity. L. Prakash et al., Pharmazie, 48: 221-222 (1993)) disclose 4-amino-5-phenyl-7-(4-aminophenyl)pyrido[2,3-d]pyrimidine, 4-amino-5-phenyl-7-(4-bromophenyl)pyrido[2,3-

d]pyrimidine, 4-amino-5-(4-methoxyphenyl)-7-(4-aminophenyl)pyrido[2,3-d]pyrimidine, and 4-amino-5-(4-methoxyphenyl)-7-(4-bromophenyl)pyrido[2,3-d]pyrimidine compounds having antifungal activity. P. Victory et al., *Tetrahedron*, 51: 10253-10258 (1995)) discloses the synthesis of 4-amino-5,7-diphenylpyrido[2,3-d]pyrimidine 5 compounds from acyclic precursors. Bridges et al.(PCT application WO 95/19774, published July 27, 1995) disclose various bicyclic heteroaromatic compounds as having utility for inhibiting tyrosine kinase of epidermal growth factors.

SUMMARY OF THE INVENTION

10 The present invention provides for 5,7-disubstituted-4-aminopyrido[2,3-d]pyrimidine compounds having utility as adenosine kinase inhibitors.

In one aspect, the present invention provides a method of inhibiting adenosine kinase by administering a compound of formula I



I,

15 or a pharmaceutically acceptable salt or amide thereof in vitro or to a mammal wherein, R¹ and R² are each independently selected from the group consisting of hydrogen, alkenyl, alkoxyalkyl, alkoxyalkylcarbonyl, alkoxy carbonyl, alkoxycarbonylalkyl, alkyl, alkylcarbonyl, aminocarbonyl, aryl, arylalkyl, arylalkylcarbonyl, arylcarbonyl, carboxyalkyl, formyl, haloalkylcarbonyl, heterocycle, heterocyclealkyl, heterocyclecarbonyl, hydroxyalkyl, iminoalkyl, and (NZ₁Z₂)alkyl, or R¹ and R² may join together with the nitrogen atom to which they are attached to form a 5-7 membered ring optionally containing 1-2 additional heteroatoms selected from the group consisting of O, N, and S;

20 Z₁ and Z₂ are each independently selected from the group consisting of hydrogen, alkoxy carbonyl, alkyl, alkylcarbonyl, benzyl, benzyloxycarbonyl, and formyl;

R^3 is selected from the group consisting of alkenyl, alkyl, alkynyl, aryl, arylalkyl, cycloalkyl, cycloalkylalkyl, heterocycle, heterocyclealkyl, heterocyclealkylcarbonyl, $(NZ_1Z_2)alkyl$, and $-R^A R^B$;

R^A is selected from the group consisting of aryl and arylalkyl;

5 R^B is selected from the group consisting of aryl, arylalkoxy, arylalkyl, aryloxy, heterocycle, and heterocyclealkyl;

R^4 is selected from the group consisting of alkenyl, alkoxyalkynyl, alkyl, alkynyl, cycloalkyl, aryl, arylalkyl, heterocycle, heterocyclealkyl, and $-R^C R^D R^E$;

R^C is selected from the group consisting of aryl, arylalkyl, heterocycle, and

10 heterocyclealkyl;

R^D is selected from the group consisting of aryl, arylalkoxy, arylalkoxyimino, arylalkyl, aryloxy, heterocycle, heterocyclealkoxy, heterocyclealkyl, heterocyclecarbonyl, heterocycleimino, heterocycleoxy, heterocycleoxyalkyl, heterocycleoxyimino, heterocycleoxyiminoalkyl, and heterocyclesulfonyl;

15 R^E is absent or selected from the group consisting of aryl, arylalkoxy, arylalkoxyimino, arylalkyl, aryloxy, heterocycle, heterocyclealkoxy, heterocyclealkyl, heterocyclecarbonyl, heterocycleimino, heterocycleoxy, heterocycleoxyalkyl, heterocycleoxyimino, heterocycleoxyiminoalkyl, and heterocyclesulfonyl; and,

20 a dashed line --- indicates that a double bond is optionally present provided that proper valencies are maintained;

with the proviso that the following compounds are excluded,

4-amino-5-(4-chorophenyl)-7-(4-nitrophenyl)pyridol[2,3-d]pyrimidine,

4-amino-5-(4-methoxyphenyl)-7-(4-nitrophenyl)pyridol[2,3-d]pyrimidine,

4-amino-5-(4-fluorophenyl)-7-(4-fluorophenyl)pyridol[2,3-d]pyrimidine,

25 4-amino-5-(4-chlorophenyl)-7-(4-fluorophenyl)pyridol[2,3-d]pyrimidine,

4-amino-5-phenyl-7-(4-aminophenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-phenyl-7-(4-bromophenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(4-methoxyphenyl)-7-(4-aminophenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(4-methoxyphenyl)-7-(4-bromophenyl)pyrido[2,3-d]pyrimidine, and

30 4-amino-5,7-diphenylpyrido[2,3-d]pyrimidine.

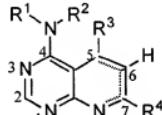
In particular, the method of inhibiting adenosine kinase comprises exposing an adenosine kinase to an effective inhibiting amount of a compound of Formula I of the present invention. Where the adenosine kinase is located in vivo, the compound is administered to the organism.

5 In still another aspect, the present invention provides a method of treating ischemia, neurological disorders, nociception, inflammation, immunosuppression, gastrointestinal dysfunctions, diabetes and sepsis in a mammal in need of such treatment, comprising administering to the mammal a therapeutically effective amount of a compound of Formula I of the present invention.

10 In a preferred aspect, the present invention provides a method of treating cerebral ischemia, myocardial ischemia, angina, coronary artery bypass graft surgery, percutaneous transluminal angioplasty, stroke, thrombotic and embolic conditions, epilepsy, anxiety, schizophrenia, pain perception, neuropathic pain, visceral pain, arthritis, sepsis, diabetes and abnormal gastrointestinal motility in a mammal in need of such treatment, comprising 15 administering to the mammal a therapeutically effective amount of a compound of Formula I of the present invention.

The present invention also contemplates the use of pharmaceutically acceptable salts and amides of compounds having Formula I.

In another aspect, the present invention provides a compound of formula I



20 I,

or a pharmaceutically acceptable salt or amide thereof wherein

R¹ and R² are each independently selected from the group consisting of hydrogen, alkenyl, alkoxyalkyl, alkoxyalkylcarbonyl, alkoxy carbonyl, alkoxycarbonylalkyl, alkyl, 25 alkylcarbonyl, aminocarbonyl, aryl, arylalkyl, arylalkylcarbonyl, arylcarbonyl, carboxyalkyl, formyl, haloalkylcarbonyl, heterocycle, heterocyclealkyl, heterocyclecarbonyl, hydroxyalkyl, iminoalkyl, and (NZ₁Z₂)alkyl, or R¹ and R² may join

together with the nitrogen atom to which they are attached to form a 5-7 membered ring optionally containing 1-2 additional heteroatoms selected from the group consisting of O, N, and S;

Z₁ and Z₂ are each independently selected from the group consisting of hydrogen,
5 alkoxy carbonyl, alkyl, alkyl carbonyl, benzyl, benzyloxy carbonyl, and formyl;

R³ is selected from the group consisting of alkenyl, alkyl, alkynyl, aryl, arylalkyl, cycloalkyl, cycloalkylalkyl, heterocycle, heterocycle alkyl, heterocycle alkyl carbonyl, (NZ₂)alkyl, and -R^AR^B;

R^A is selected from the group consisting aryl and arylalkyl;

10 R^B is selected from the group consisting of aryl, arylalkoxy, arylalkyl, aryloxy, heterocycle, and heterocycle alkyl;

R⁴ is selected from the group consisting of alkenyl, alkoxy alkynyl, alkyl, alkynyl, cycloalkyl, aryl, arylalkyl, heterocycle, heterocycle alkyl, and -R^CR^DR^E;

R^C is selected from the group consisting of aryl, arylalkyl, heterocycle, and
15 heterocycle alkyl;

R^D is selected from the group consisting of aryl, arylalkoxy, arylalkoxyimino, arylalkyl, aryloxy, heterocycle, heterocycle alkoxyl, heterocycle alkyl, heterocycle carbonyl, heterocycle imino, heterocycle oxy, heterocycle oxyalkyl, heterocycle oxyimino, heterocycle oxyiminoalkyl, and heterocyclesulfonyl;

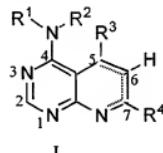
20 R^E is absent or is selected from the group consisting of aryl, arylalkoxy, arylalkoxyimino, arylalkyl, aryloxy, heterocycle, heterocycle alkoxyl, heterocycle alkyl, heterocycle carbonyl, heterocycle imino, heterocycle oxy, heterocycle oxyalkyl, heterocycle oxyimino, heterocycle oxyiminoalkyl, and heterocyclesulfonyl; and
a dashed line --- indicates that a double bond is optionally present provided that
25 proper valencies are maintained;

with the proviso that the compound may not be selected from the group consisting of:
4-amino-5-(4-chlorophenyl)-7-(4-nitrophenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(4-methoxyphenyl)-7-(4-nitrophenyl)pyrido[2,3-d]pyrimidine;
30 4-amino-5-(4-fluorophenyl)-7-(4-fluorophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(4-chlorophenyl)-7-(4-fluorophenyl)pyrido[2,3-d]pyrimidine;
 4-amino-5-phenyl-7-(4-aminophenyl)pyrido[2,3-d]pyrimidine;
 4-amino-5-phenyl-7-(4-bromophenyl)pyrido[2,3-d]pyrimidine;
 4-amino-5-(4-methoxyphenyl)-7-(4-aminophenyl)pyrido[2,3-d]pyrimidine;
 5 4-amino-5-(4-methoxyphenyl)-7-(4-bromophenyl)pyrido[2,3-d]pyrimidine; and
 4-amino-5,7-diphenylpyrido[2,3-d]pyrimidine.

In another aspect, the present invention provides a pharmaceutical composition comprising a therapeutically effective amount of a compound of Formula I above in combination with a pharmaceutically acceptable carrier.

10 In another aspect, the present invention provides a process for the preparation of adenosine kinase inhibiting compounds of formula I



wherein

15 R¹ and R² are hydrogen;

R³ is selected from the group consisting of alkenyl, alkyl, alkynyl, aryl, arylalkyl, cycloalkyl, cycloalkylalkyl, heterocycle, heterocyclealkyl, heterocyclealkylcarbonyl, (NZ₁Z₂)alkyl, and -R^AR^B;

20 R^A is selected from the group consisting aryl and arylalkyl;

R^B is selected from the group consisting of aryl, arylalkoxy, arylalkyl, aryloxy, heterocycle, and heterocyclealkyl;

R⁴ is selected from the group consisting of alkenyl, alkoxyalkynyl, alkyl, alkynyl, cycloalkyl, aryl, arylalkyl, heterocycle, heterocyclealkyl, and -R^CR^DR^E;

25 R^C is selected from the group consisting of aryl, arylalkyl, heterocycle, and heterocyclealkyl;

R^D is selected from the group consisting of aryl, arylalkoxy, arylalkoxyimino, aryalkyl, aryloxy, heterocycle, heterocyclealkoxy, heterocyclealkyl, heterocyclecarbonyl,

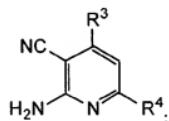
heterocycleimino, heterocycloxy, heterocycloxyalkyl, heterocycloxyimino, heterocycloxyiminoalkyl, and heterocyclesulfonyl; and

R^E is absent or is selected from the group consisting of aryl, arylalkoxy, arylalkoxyimino, arylalkyl, aryloxy, heterocycle, heterocylealkoxy, heterocyclealkyl, 5 heterocyclecarbonyl, heterocycleimino, heterocycloxy, heterocycloxyalkyl, heterocycloxyimino, heterocycloxyiminoalkyl, and heterocyclesulfonyl; and

a dashed line --- indicates that a double bond is optionally present provided that proper valencies are maintained;

the method comprising

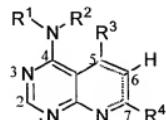
10 (a) reacting a ketone having the formula $R^4\text{-CO-CH}_3$, wherein R^4 is as defined above, with an aldehyde having the formula $R^3\text{-CHO}$, wherein R^3 is as defined above and malononitrile in the presence of an ammonium salt under anhydrous conditions and isolating a first intermediate compound having the structure



15 (b) reacting the first intermediate compound with formamide at reflux for from about 1 to about 8 hours, and isolating the compound of formula I which has a double bond between the 5,6 carbons and a double bond between the 7 carbon and the 8 nitrogen, and then,

(c) optionally reducing the compound from step (b) to form a partially reduced or fully reduced right side of formula I by catalytic hydrogenation.

20 In another aspect, the present invention provides a process for the preparation of adenosine kinase inhibiting compounds of formula I



I,

wherein

R¹ and R² are hydrogen;

R³ is selected from the group consisting of alkaryl, alkyl, alkynyl, aryl, arylalkyl, cycloalkyl, cycloalkylalkyl, heterocycle, heterocyclealkyl, heterocyclealkylcarbonyl, (NZ₁Z₂)alkyl, and -R^AR^B;

5 R^A is selected from the group consisting of aryl and arylalkyl;

R^B is selected from the group consisting of aryl, arylalkoxy, arylalkyl, aryloxy, heterocycle, and heterocyclealkyl;

R⁴ is selected from the group consisting of alkenyl, alkoxyalkynyl, alkyl, alkynyl, cycloalkyl, aryl, arylalkyl, heterocycle, heterocyclealkyl, and -R^CR^DR^E;

10 R^C is selected from the group consisting of aryl, arylalkyl, heterocycle, and heterocyclealkyl;

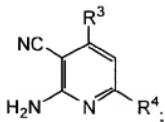
R^D is selected from the group consisting of aryl, arylalkoxy, arylalkoxyimino, arylalkyl, aryloxy, heterocycle, heterocyclealkoxy, heterocyclealkyl, heterocyclecarbonyl, heterocycleimino, heterocycloxy, heterocycloxyalkyl, heterocycloxyimino, 15 heterocycloxyiminoalkyl, and heterocyclesulfonyl; and

R^E is absent or is selected from the group consisting of aryl, arylalkoxy, arylalkoxyimino, arylalkyl, aryloxy, heterocycle, heterocyclealkoxy, heterocyclealkyl, heterocyclecarbonyl, heterocycleimino, heterocycloxy, heterocycloxyalkyl, heterocycloxyimino, heterocycloxyiminoalkyl, and heterocyclesulfonyl; and

20 a dashed line --- indicates that a double bond is optionally present provided that proper valencies are maintained;

the method comprising

(a) reacting a ketone having the formula R⁴C(O)CH₃, wherein R⁴ is as defined above, with an dicyanoalkene compound having the formula R³CH=C(CN)₂, wherein R³ is as defined above by heating at reflux and isolating a first intermediate compound having the structure



(b) reacting the first intermediate compound with formamide at reflux for from about 1 to about 8 hours, and isolating the compound of formula I which has a double bond between the 5 and 6 carbons and a double bond between the 7 carbon and the 8 nitrogen and

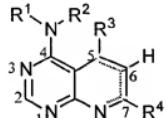
5 (c) optionally reducing the compound from step (b) to form a partially reduced or fully reduced right side of formula I by catalytic hydrogenation.

DETAILED DESCRIPTION OF THE INVENTION

The present invention relates to 5,7-disubstituted-4-aminopyrido[2,3-d]pyrimidine compounds that are useful in inhibiting adenosine kinase, to pharmaceutical compositions containing such compounds, to a method of using such compounds for inhibiting adenosine kinase, to novel 5,7-disubstituted-4-aminopyrido[2,3-d]pyrimidine compounds and to a process of preparing 5,7-disubstituted-4-aminopyrido[2,3-d]pyrimidine compounds.

15 In one aspect, the present invention provides 5,7-disubstituted-4-aminopyrido[2,3-d]pyrimidine compounds that are adenosine kinase inhibitors. An adenosine kinase inhibitor of the present invention is a compound of the Formula I, shown above.

As summarized above, the present invention relates to a method of inhibiting adenosine kinase comprising administering a compound of formula I



1

wherein

R^1 and R^2 are independently selected from the group consisting of hydrogen, alkenyl, alkoxyalkyl, alkoxyalkylcarbonyl, alkoxycarbonyl, alkyl, alkylcarbonyl, aminocarbonyl, aryl, arylcarbonyl, carboxyalkyl, formyl, haloalkylcarbonyl, heterocyclealkyl, hydroxyalkyl, iminoalkyl, and $(N_2Z_2)alkyl$, or R^1 and R^2 may join together with the nitrogen atom to which they are attached to form a 6 membered ring

optionally containing 1 additional heteroatom selected from the group consisting of O, N, and S;

R³ is selected from the group consisting of alkenyl, alkyl, aryl, arylalkyl, cycloalkyl, heterocycle, heterocyclealkyl, (N₂Z₂)alkyl, and -R^AR^B;

5 R^A is selected from the group consisting of aryl and arylalkyl;

R^B is selected from the group consisting of aryl, arylalkoxy, arylalkyl, aryloxy, and heterocycle;

R⁴ is selected from the group consisting of alkoxyalkynyl, alkynyl, aryl, heterocycle, and -R^CR^DR^E;

10 R^C is selected from the group consisting of aryl and heterocycle;

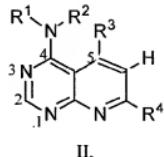
R^D is selected from the group consisting of aryl, arylalkoxy, arylalkyl, aryloxy, heterocycle, heterocyclealkoxy, heterocyclealkyl, heterocyclecarbonyl, heterocycleoxy, and heterocyclesulfonyl;

R^E is absent or selected from the group consisting of aryl, arylalkoxy,

15 arylalkoxyimino, arylalkyl, aryloxy, heterocycle, heterocyclealkoxy, heterocyclealkyl, heterocyclecarbonyl, heterocycleimino, heterocycleoxy, heterocycleoxyalkyl, heterocycleoxyimino, and heterocycleoxyiminoalkyl; and

a dashed line --- indicates that a double bond is optionally present provided that proper valencies are maintained.

20 The preferred compounds utilized in the above method of inhibiting adenosine kinase are selected from a compound of formula II



wherein

25 R¹ and R² are each independently selected from the group consisting of hydrogen, alkenyl, alkoxyalkyl, alkoxyalkylcarbonyl, alkoxy carbonyl, alkyl, alkylcarbonyl, aminocarbonyl, aryl, arylcarbonyl, carboxyalkyl, formyl, haloalkylcarbonyl,

heteroclealkyl, hydroxyalkyl, iminoalkyl, and (NZ₁Z₂)alkyl, or R¹ and R² may join together with the nitrogen atom to which they are attached to form a 6 membered ring optionally containing 1 additional heteroatom selected from the group consisting of O, N, and S;

5 R³ is selected from the group consisting of alkenyl, alkyl, aryl, arylalkyl, cycloalkyl, heterocycle, heteroclealkyl, (NZ₁Z₂)alkyl, and -R^AR^B;
R^A is selected from the group consisting of aryl and arylalkyl;
R^B is selected from the group consisting of aryl, arylalkoxy, arylalkyl, aryloxy, and heterocycle;

10 R⁴ is selected from the group consisting of alkoxyalkynyl, alkynyl, aryl, heterocycle, and -R^CR^DR^E;
R^C is selected from the group consisting of aryl and heterocycle;
R^D is selected from the group consisting of aryl, arylalkoxy, arylalkyl, aryloxy, heterocycle, heteroclealkoxy, heteroclealkyl, heteroclecarbonyl, heterocleoxy, and heterocyclesulfonyl; and

15 R^E is absent or is selected from the group consisting of aryl, arylalkoxy, arylalkoxyimino, arylalkyl, aryloxy, heterocycle, heteroclealkoxy, heteroclealkyl, heteroclecarbonyl, heterocleimino, heterocleoxy, heterocleoxyalkyl, heterocleoxyimino, and heterocleoxyiminoalkyl.

20 In a preferred embodiment, an adenosine kinase inhibitor of the present invention is a compound of Formula II above, wherein R⁴ is aryl or heterocycle and substituted versions thereof or -R^CR^DR^E.

25 In a more preferred embodiment, an adenosine kinase inhibitor of the present invention is a compound of Formula II above, wherein R⁴ is aryl or heterocycle and substituted versions thereof and R³ is alkyl, aryl, arylalkyl or heterocycle and substituted versions thereof wherein the substituents are as identified above.

30 In another preferred embodiment, an adenosine kinase inhibitor of the present invention is a compound of Formula I above, wherein R⁴ is selected from the group consisting of: phenyl; thiophene-2-yl; 3-methyl-2-oxobenzoxazolin-6-yl; 2-(dimethylamino)-5-pyrimidinyl; 2-(N-formyl-N-methyl amino)-5-pyrimidinyl; 2-(N-

methoxyethyl-N-methyl amino)-5-pyrimidinyl; 2-(N-methylamino)-5-pyrimidinyl; 2-(1-morpholinyl)-5-pyrimidinyl; 2-(1-pyrrolidinyl)-5-pyrimidinyl; 2-dimethylamino-5-pyrimidinyl; 2-furanyl; 2-oxobenzoxazolin-6-yl; 2-pyridyl; 3-(dimethylamino)phenyl; 3-amino-4-methoxyphenyl; 3-bromo-4-(dimethylamino)phenyl; 3-methoxyphenyl; 3-
5 methyl-4-(N-acetyl-N-methylamino)phenyl; 3-methyl-4-(N-formyl-N-methylamino)phenyl; 3-methyl-4-(N-methyl-N-(trifluoroacetyl)amino)phenyl; 3-methyl-4-(N-methylamino)phenyl; 3-methyl-4-pyrrolidinylphenyl; 3-pyridyl; 3,4-dichlorophenyl; 3,4-methylenedioxypyphenyl; 3,4,5-trimethoxyphenyl; 4-(acetylamino)phenyl; 4-(dimethylamino)-3-fluorophenyl; 4-(dimethylamino)phenyl; 4-(imidazol-1-yl)phenyl; 4-
10 (methylthio)phenyl; 4-(morpholinyl)phenyl; 4-(N-(2-(dimethylamino)ethyl)amino)phenyl; 4-(N-(2-methoxyethyl)amino)phenyl; 4-(N-acetyl-N-methylamino)phenyl; 4-(N-ethyl-N-formylamino)phenyl; 4-(N-ethylamino)phenyl; 4-(N-formyl-N-(2-methoxyethyl)amino)phenyl; 4-(N-isopropylamino)phenyl; 4-(N-methyl-N-(2-dimethylamino)ethyl)amino)phenyl; 4-(N-methyl-N-(2-
15 phthalimidyl)acetyl)amino)phenyl; 4-(N-methyl-N-(2-cyano)ethylamino)phenyl; 4-(N-methyl-N-(2-methoxyethyl)amino)phenyl; 4-(N-methyl-N-(3-methoxy)propionylamino)phenyl; 4-(N-methyl-N-acetylamino)phenyl; 4-(N-methyl-N-formylamino)phenyl; 4-(N-methyl-N-trifluoroacetylamino)phenyl; 4-(N-morpholinyl)phenyl; 4-(thiophene-2-yl)phenyl; 4-(ureido)phenyl; 4-(2-
20 (dimethylamino)acetylamino)phenyl; 4-(2-(2-methoxyacetylamino)ethyl)amino)phenyl; 4-(2-methoxyethoxyphenyl; 4-(2-oxo-3-oxazolidinyl)phenyl; 4-(4-methoxy-2-butyl)phenyl; 4-(4-methylpiperidinyl)phenyl; 4-(5-pyrimidinyl)phenyl; 4-aminophenyl; 4-bromophenyl; 4-butoxyphenyl; 4-carboxamidophenyl; 4-chlorophenyl; 4-cyanophenyl; 4-diethylaminophenyl; 4-diethylmalonylallylphenyl); 4-dimethylaminophenyl; 4-
25 ethoxyphenyl; 4-ethylphenyl; 4-fluorophenyl; 4-hydroxyphenyl; 4-imidazolylphenyl; 4-iodophenyl; 4-isopropylphenyl; 4-methoxyphenyl; 4-methylaminophenyl; 4-methylsulfonylphenyl; 4-morpholinylphenyl; 4-N-(2-(dimethylamino)ethyl)-N-formylamino)phenyl; 4-N-(3-methoxypropionyl)-N-isopropyl-amino)phenyl; 4-N-ethyl-N-(2-methoxyethyl)amino)phenyl; 4-N-formylpiperazinylphenyl; 4-nitrophenyl; 4-
30 piperidinylphenyl; 4-(3-pyridyl)phenyl; 4-pyrrolidinylphenyl; 4-t-butylacrylphenyl; 5-

(dimethylamino)thiophene-2-yl; 5-amino-2-pyridyl; 5-dimethylamino-2-pyrazinyl; 3-dimethylaminopyridin-6-yl; 5-dimethylamino-2-pyridyl; 5-pyrimidinylphenyl; 6-(N-methyl-N-formylamino)-3-pyridinyl; 6-(N-methyl-N-methoxyethylamino)-3-pyridinyl; 6-(2-oxo-3-oxazolidinyl)-3-pyridinyl; 6-dimethylamino-3-pyridinyl; 6-imidazolyl-3-pyridinyl; 6-morpholinyl-3-pyridinyl; 6-pyrrolidinyl-3-pyridinyl; 6-(2-propyl)-3-pyridinyl; 6-(4-formylamino)phenyl; 6-(4-oxopiperidinyl)-3-pyridazinyl; 6-(4-morpholinyliminopiperidinyl)-3-pyridazinyl; 6-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptan-5-yl)-3-pyridazinyl; 6-(4-methoxyiminopiperidinyl)-3-pyridazinyl; 6-phenylmethoxy-3-pyridazinyl; 6-(1,1-dioxidothiazolidin-3-yl)-3-pyridyl; 6-(1,3-dioxa-8-azaspiro[4.5]decan-8-yl)-3-pyridyl; 6-(1-oxa-4-thia-8-azaspiro[4.5]decan-8-yl)-3-pyridyl; 6-(1,1-dioxidothiomorpholinyl)-3-pyridazinyl; 6-(1-oxa-4,4-dioxido-4-thia-8-azaspiro[4.5]decan-8-yl)-3-pyridyl; 6-(1-oxa-4-oxo-4-thia-8-azaspiro[4.5]decan-8-yl)-3-pyridyl; 6-(3-hydroxy-8-azabicyclo[3.2.1]octan-8-yl)-3-pyridyl; 6-(4-oxo-1-phenyl-1,3,8-triazaspiro[4.5]decan-8-yl)-3-pyridyl; 6-(4-oxo-1-phenyl-1,3,8-triazaspiro[4.5]decan-2-yl)-3-pyridyl; 6-(N-1,4-dioxa-8-azaspiro[4.5]decan-8-yl)-3-pyridylsulfonamide; 2-(1,1-dioxidothiomorpholinyl)-5-thiazoyl; 5-(1,4-dioxa-8-azaspiro[4.5]decan-8-yl)-2-pyrazinyl; 2-(1,4-dioxa-8-azaspiro[4.5]decan-8-yl)-5-thiazoyl; 6-(hexahydro-1H-furo[3,4-c]pyrrol-5-yl)-3-pyridazinyl; 6-(hexahydro-1H-furo[3,4-c]pyrrol-5-yl)-3-pyridyl; 6-(4-methoxypiperidinyl)-3-pyridyl; 6-(4,7-epoxy-7-methyl-2,3,3A,4,5,6,7,7a-octahydro-1H-isoindolyl)-3-pyridazinyl; 6-(4-(4-tetrahydropyranlyoxy)iminopiperidinyl)-3-pyridazinyl; 6-isopropoxy-3-pyridazinyl; 6-(2,4-dioxo-(1H,3H)-quinazolin-3-yl)-3-pyridyl; 6-(4-(N-methylpiperazinyl)iminopiperidinyl)-3-pyridazinyl; 6-(4-tetrahydropyranlyoxy)-3-pyridazinyl; 6-morpholinylethoxy-3-pyridazinyl; 6-(4-ethoxypiperidinyl)-3-pyridazinyl; 6-(1,4-dioxa-8-azaspiro[4.5]decan-8-yl)-3-pyridyl; 6-(4-(2-ethoxyethoxy)piperidinyl)-3-pyridazinyl; 6-(3aR,6aS)-2-oxo-tetrahydro-3aH-[1,3]dioxolo[4,5-c]pyrrol-5-yl)-3-pyridyl; 6-(4-(4-tetrahydropyranlyoxyethyl)piperidinyl)-3-pyridazinyl; 6-(3-(R)-tetrahydrofuranlyoxy)piperidinyl)-3-pyridazinyl; 6-(3-(S)-tetrahydrofuranlyoxy)piperidinyl)-3-pyridazinyl; 6-(trans-3-ethoxy-4-hydroxy)pyrrolidinyl)-3-pyridazinyl; 6-(cis-3-ethoxy-4-hydroxy)pyrrolidinyl)-3-pyridazinyl; 6-(trans-3-ethoxy-4-hydroxy)pyrrolidinyl)-3-pyridyl; 6-(trans-3,4-bis-

ethoxy)pyrrolidinyl)-3-pyridazinyl; 6-(trans-3,4-bis-ethoxy)pyrrolidinyl)-3-pyridyl; 6-(cis-3,4-bis-ethoxy)pyrrolidinyl)-3-pyridyl; 6-(cis-3,4-bis-ethoxy)pyrrolidinyl)-3-pyridazinyl; 6-(cis-3-ethoxy-4-hydroxy)pyrrolidinyl)-3-pyridyl; 6-(cis-3-amino-4-hydroxy)pyrrolidinyl)-3-pyridyl; 6-(1,5-dioxa-9-azaspiro[5.5]undecan-9-yl)-3-pyridazinyl; 6-(4-tertbutyl)piperidinyl-3-pyridazinyl; 6-(4-N-formyl)piperidinyl-3-pyridazinyl; 6-morpholinyl-3-pyridazinyl; 4-N-1,4-dioxa-8-azaspiro[4.5]decan-8-ylbenzenesulfonamide; 4-(4-dioxa-8-azaspiro[4.5]decan-8-ylcarboxamide)phenyl; 6-(3-methoxy-1,5-dioxa-9-azaspiro[5.5]undecan-9-yl)-3-pyridazinyl; 6-(1,5-dioxa-3-hydroxymethyl-9-azaspiro[5.5]undecan-9-yl)-3-pyridazinyl; 6-(S-O-ethyl-2-hydroxymethylpyrrolidinyl)-3-pyridazinyl; 6-(4-acetyl-1-oxa-4,8-diazaspiro[4.5]decan-8-yl)-3-pyridazinyl; 6-((2R,3R)-2,3-bis(methoxymethyl)-1,4-dioxa-8-azaspiro[4.5]decan-8-yl)-3-pyridazinyl; 6-((2S,3S)-2,3-dimethyl-1,4-dioxa-8-azaspiro[4.5]decan-8-yl)-3-pyridazinyl; 6-(4,4-(cis-1,2-dioxycyclopentane)piperidinyl)-3-pyridazinyl; 6-(4,4-(1S,2S-dimethoxymethylethanedioxy)piperidinyl)-3-pyridazinyl; 6-(4,4-(cis-3,4-dioxy-oxacyclopentane)piperidinyl)-3-pyridazinyl; 6-(4,4-(1,3-dioxy-2-methoxypropylene)piperidinyl)-3-pyridazinyl; 6-(4,4-(1,3-dioxy-2-hydroxymethylpropylene)piperidinyl)-3-pyridazinyl; 6-(4,4-(2-(2,2-spiro-oxacyclopropane-1,3-dioxypropylene)piperidinyl)-3-pyridazinyl; 6-morpholinyl-3-pyridazinyl; 6-(4-morpholinyliminopiperidinyl)-3-pyridyl; 6-(4-(N-methylpiperazinyl)iminopiperidinyl)-3-pyridyl; 6-(4-(1,2,4-triazol-1-yl)iminopiperidinyl)-3-pyridyl; 6-(4-ethylpiperidinylcarboxylate)-3-pyridyl; 2-phenylmethyl-3(2H)-pyridazinone-6-yl; 6-(4-(morpholinylcarboxamide)piperidinyl)-3-pyridyl; 6-(4-(N-morpholinylaminocarboxamide)piperidinyl)-3-pyridyl; 6-(4-(N,N-dimethylaminocarboxamide)piperidinyl)-3-pyridyl; 6-(4-(N-methyl-N-methoxyethylcarboxamide)piperidinyl)-3-pyridyl; 6-(4-(N-methoxyethylcarboxamide)piperidinyl)-3-pyridyl; 6-(4-hydroxymethylpiperidinyl)-3-pyridyl; 6-(4-hydroxypiperidinyl)-3-pyridyl; 6-(4-N-acetylpirerazinyl)-3-pyridyl; 6-(4-cyanopiperidinyl)-3-pyridyl; 6-(4-N-(4-fluorophenyl)piperazinyl)-3-pyridyl; 4-morpholinylbenzenesulfonamide; 4-N-4,4-ethylenedioxypiperidinylbenzenesulfonamide;

4-N-cyclopropylbenzenesulfonamide; 4-piperidinebenzenesulfonamide; 4-(4-cyanopiperidine)benzenesulfonamide; 4-N-cyclopropylmethylbenzenesulfonamide; 4-N,N-dimethylaminobzenesulfonamide; 4-N-(S)-2-hydroxymethylpyrrolidincbenzenesulfonamide; 4-(4-5 hydroxypiperidine)benzenesulfonamide; 4-(cis-3,5-dimethylmorpholinyl)benzenesulfonamide; 3-fluoro-4-thiomorpholinylphenyl; 6-(thiomorpholinyl)-3-pyridyl; 6-(4,4-dioxothiomorpholinyl)-3-pyridyl; 4-(4,4-ethylenedioxypiperidinylcarboxamide)phenyl; 4-(N-cyclopropylcarboxamide)phenyl; 4-(morpholinylcarboxamide)phenyl; 6-N-cyclopropylamino-3-pyridyl; 4-(4-10 hydroxypiperidinylcarboxamide)phenyl; 6-(S)-hydroxymethylpyrrolidinyl-3-pyridazinyl; 6-(4-(2-ethoxyethoxy)piperidinyl)-3-pyridyl; 6-hexahydropyrimidine)-3-pyridyl; 6-(S)-2-ethoxyethoxyppyrrolidinyl)-3-pyridyl; 6-(R)-2-ethoxyethoxyppyrrolidinyl)-3-pyridyl; 6-(cis-15 3,4-dihydroxypyridolinyl)-3-pyridyl; 6-[(3aR,6aS)-tetrahydro-3aH-[1,3]dioxolo[4,5-c]pyrrol-2-one-5-yl]-3-pyridyl; 6-(cis-2,3-dihydroxypyrrrolidinyl)-3-pyridazinyl; 6-(S,R-2-hydroxymethyl-4-hydroxypyrrrolidinyl)-3-pyridyl; 6-(R-2-hydroxymethyl-4-pyrrolidinyl)-3-pyridazinyl; 6-(1S,4S)-2-aza-5-oxa-bicyclo[2.2.1]heptane)-3-pyridyl; 6-(2-imidizolidone-1-yl)-3-pyridyl; 4-(2,4-(1H,3H)-quinazolinedion-3-yl)phenyl; 6-morpholinylcarboxamide-3-pyridazinyl; 6-methoxy-3-pyridazinyl; 6-N,N-diethoxyethylamino-3-pyridazinyl; 6-(4-ethoxymethylpiperidinyl)-3-pyridazinyl; 6-(4-20 tetrahydropyranylmethyl)piperidinyl)-3-pyridazinyl; 6-(4-ethoxyethoxymethylpiperidinyl)-3-pyridazinyl; 6-N-methyl-N-1,3-dioxalanemethylamino)-3-pyridazinyl; 6-(4,4-dioxyethylenecyclohexyloxy)-3-pyridazinyl; 6-dihydroxymethylmethoxy-3-pyridazinyl; 6-(3-pyridyloxy)-3-pyridazinyl; 4,7-epoxy-7-methyl-2,3,3A,4,5,6,7,7a-octahydro-1H-isoindolyl; 6-(4-N-methyl-N-methoxyethyl)-3-pyridazinyl; 6-(3,4-dimethoxymethoxypyrrrolidinyl)-3-pyridazinyl; 6-(trans-3-hydroxy-4-methylpyrrolidinyl)-3-pyridyl; 6-(cis-3-hydroxy-4-methylpyrrolidinyl)-3-pyridazinyl; 6-(cis-3-hydroxy-4-methylpyrrolidinyl)-3-pyridyl; 6-(trans-3-cyano-4-hydroxypyrrrolidinyl)-3-pyridyl; 6-(3-hydroxy-4-tert-butylcarboxamidepyrrolidinyl)-3-pyridyl; 6-(S-2-(4-25 tetrahydropyranlyoxy)methylpyrrolidinyl)-3-pyridazinyl; 6-(2-(4-

tetrahydropyranloxy)iminopyrrolidinyl)-3-pyridazinyl; 2-morpholinyl-5-thiazoyl; 5-bromo-2-thienyl; 2,5-dimethyl-3-thienyl; 5-chloro-2-thienyl; 2,4-dimethyl-5-thiazoyl; 5-methyl-2-thienyl; 2-furanyl; 2-(4,4-dioxyethylenepiperidinyl)-5-thiazoyl; 3-thienyl; 3-methyl-2-thienyl; 2-morpholinyl-4-thiazoyl; 2-morpholinyl-4-trifluoromethyl-5-thiazoyl;

5 5-morpholinyl-2-thienyl; 4-methyl-2-morpholinyl-5-thiazoyl; 2,5-dichloro-3-thienyl; 2,5-dimethyl-3-furanyl; N-methyl-2-pyrrolyl; 2-N,N-dimethylamino-5-thiazoyl; 2-morpholinyl-5-thiazoyl; 2-(4,4-dioxythiomorpholinyl)-5-thiazoyl; 1-N-methyl-2-morpholinyl-5-imidazoyl; 2-morpholinyl-5-oxazoyl; 2-N-methyl-N-methoxyethylamino-5-thiazoyl; 2-N-methyl-N-ethylamino-5-thiazoyl; 2-N-pyrrolidinyl-5-thiazoyl; 2-N-methyl-N-propylamino-5-thiazoyl; 2-N,N-diethylamino-5-thiazoyl; 2-(N-methylpiperazinyl)-5-thiazoyl; 2-(N-(2-pyridyl)piperazinyl)-5-thiazoyl; 2-N-methy-N-(2-pyridylethyl)-5-thiazoyl; 2-(4-oxopiperazinyl)-5-thiazoyl; 2-(4-(N-morpholiny)iminopiperazinyl)-5-thiazoyl; 6-N-morpholine-3-pyridinesulfonamide; 2-(4-oxopiperidinyl)-5-pyrimidyl; 2-(4,4-dioxyethylenepiperidinyl)-5-pyrimidyl; 5-(4,4-dioxethylenepiperidinyl)-2-pyrazinyl; 5-(4-oxopiperidinyl)-2-pyrazinyl; 6-N-cyclopropyl-3-pyridinesulfonamide; 6-N-(4,4-dioxethylenepiperidinyl)-3-pyridinesulfonamide; 2-(4-(4-tetrahydropyranloxy)iminopiperidinyl)-5-pyrazinyl; 6-(4-(phenylmethoxy)iminopiperidinyl)-3-pyridyl; 6-(4-(tert-butylloxy)iminopiperidinyl)-3-pyridyl; 6-(4-(cyclohexoxyloxy)iminopiperidinyl)-3-pyridyl; 6-(4-hydroxyiminopiperidinyl)-3-pyridyl; 6-(4-(4-tetrahydropyranloxy)iminopiperidinyl)-3-pyridyl; 6-(4-methoxyethoxyiminopiperidinyl)-3-pyridyl; 6-(4-(2-phenylmethoxy)iminopiperidinyl)-3-pyridyl; 6-(4-(4'-(5'H-2-oxufuranyl)-4-hydroxy)piperidinyl)-3-pyridyl; 6-(4-(1-(4-tetrahydropyranloxy)iminoethyl)-4-hydroxypiperidinyl)-3-pyridazinyl; 6-(4-(4'-acetyl-4'-hydroxypiperidinyl)-3-pyridazinyl; 6-(4-(1-(isopropylcarboxymethoxy)iminoethyl))-4-hydroxypiperidinyl)-3-pyridyl; 6-(4-(1-(isopropylcarboxymethoxy)iminoethyl))-4-hydroxypiperidinyl)-3-pyridyl; 6-(4-(1-(ethylcarboxymethoxy)iminoethyl))-4-hydroxypiperidinyl)-3-pyridyl; 6-(4-(1-(methylcarboxymethoxy)iminoethyl))-4-hydroxypiperidinyl)-3-pyridyl; 6-(4-(1-(2-tetrahydropyranloxy)iminoethyl))-4-hydroxypiperidinyl)-3-pyridyl; 6-(4-(1-(allyloxy)iminoethyl))-4-hydroxypiperidinyl)-3-pyridyl; 6-(4-(1-(ethoxy)iminoethyl))-4-hydroxypiperidinyl)-3-pyridyl; 6-(4-(1-(methoxy)iminoethyl))-4-hydroxypiperidinyl)-3-pyridyl; 6-(4-(1-(hydroxy)iminoethyl))-4-hydroxypiperidinyl)-3-pyridyl;

hydroxypiperidinyl)-3-pyridyl; 6-(4-(2-tetrahydropyranloxy)iminopiperidinyl)-3-pyridyl; 6-(4-(isopropylcarboxymethoxy)iminopiperidinyl)-3-pyridyl; 6-(4-hydroxy-4-(1-(4-tetrahydropyranloxy)iminoethyl))-4-hydroxypiperidinyl)-3-pyridyl; 6-(4-(3-butyrolactone)-4-hydroxypiperidinyl)-3-pyridyl; 6-(4-(2-butyrolactone)-4-5 hydroxypiperidinyl)-3-pyridazinyl; 6-(4-acetyl-4-hydroxypiperidinyl)-3-pyridyl; 6-(3-hydroxyazetidinyl)-3-pyridyl; 6-(cis-3-hydroxytropanyl)-3-pyridyl; 6-(cis-2,3-dihydroxypiperidinyl)-3-pyridyl; 6-(N-methyl-N-(3-pyridylmethyl)amino)-3-pyridazinyl; 6-(1,2,3,6-tetrahydropyridyl)-3-pyridyl; 6-(4-(N-4'-methoxyphenylcarbamoyl)piperidinyl)-3-pyridazinyl; 6-(4-(2-butyrolactone)-4-hydroxypiperidinyl)-3-pyridyl; 6-(trans-3,4-bis(N-10 4'-methoxyphenylcarbamoyl)pyrrolidinyl)-3-pyridyl; 6-(trans-3-hydroxytropanyl)-3-pyridyl; 6-(S,S-trans-3,4-dihydroxy pyrrolidinyl)-3-pyridyl; 6-(R,R-trans-3,4-dihydroxypyrrolidinyl)-3-pyridyl; 6-(8-(1-phenyl-1,3,8-triaza-2-spiro[4.5]deceN-4-one)-3-pyridyl; 6-(8-(1-phenyl-1,3,8-triaza-2-spiro[4.5]deceN-4-one)-3-pyridyl; 6-(4-(2-keto-1-benzimidazolinyl)piperidinyl)-15 3-pyridazinyl; 6-(4-oxothiomorpholinyl)-3-pyridyl; 6-(4-(2-keto-1-benzimidazolinyl)piperidinyl)-3-pyridyl; 6-(N-methyl-N-(2-pyridylethyl)amino)-3-pyridyl; 6-(N-methyl-N-(4-pyridylethyl)amino)-3-pyridyl; 6-N-(3-pyridylmethyl)amino-3-pyridyl; 6-(2-hydroxymethylpiperidinyl)-3-pyridyl; 6-(4-hydroxy-4-(4-bromophenyl)piperidinyl)-3-pyridyl; 6-(4-N-(2-pyridyl)piperazinyl)-3-pyridyl; 6-(4-N-20 (2-hydroxyethoxyethyl)piperazinyl)-3-pyridyl; 6-(4,4-diacetoxyethylthio)piperidinyl)-3-pyridyl; 6-(N-methy-N-(3-pyridylmethyl)amino)-3-pyridyl; 6-(4-pyrrolidinyl)piperidinyl)-3-pyridyl; 6-(4-N-cyanomethylpiperazinyl)-3-pyridyl; 6-(3-hydroxypyrrrolidinyl)-3-pyridyl; 6-(4-methylpiperidinyl)-3-pyridyl; 6-(cis-3,5-dimethylmorpholinyl)-3-pyridyl; 6-(4,4-difluoropipridinyl)-3-pyridyl; 6-(4,4-dioxythiomorpholinyl)-3-pyridazinyl; 6-25 thiazolidinyl-3-pyridyl; 6-(1,1-dioxythiazolidinyl)-3-pyridyl; 6-thiomorpholinyl-3-pyridazinyl; 6-(2,5-dihydropyrrrolyl)-3-pyridyl; 6-hydroxy-3-pyridazinyl; 6-piperidinyl-3-pyridyl; and 6-(4-tetrahydropyranloxy)iminopyrrolidinyl-3-pyridyl; 6-morpholinyl-3-pyridyl.

In another preferred embodiment, an adenosine kinase inhibitor of the present invention is a compound of Formula I above, wherein R³ is selected from the group

consisting of: (thiophene-2-yl)methyl; (thiophene-3-yl)methyl; butyl; cycloheptyl; pentyl; thiophene-2-yl; 1-(3-bromophenyl)ethyl; 2-(N-phenylmethoxycarbonyl)aminophenyl; 2-(3-bromophenyl)ethyl; 2-(3-cyanophenyl)methyl; 2-(4-bromophenyl)ethyl; 2-(5-chloro-2-(thiophen-3-yl)phenyl; 2-bromophenyl; 2-furanyl; 2-methylpropyl; 2-phenylethyl; 5 phenylmethyl; 2,3-dimethoxyphenyl; 2,3-methylenedioxyphenyl; 3-(furan-2-yl)phenyl; 3-(thiophen-2-yl)phenyl; 3-(2-pyridyl)phenyl; 3-(3-methoxybenzyl)phenyl; 2-(3-aminopropynyl)phenylmethyl; 3-benzylxyphenyl; 3-bromo-4-fluorophenyl; 3-bromo-5-iodophenyl; 3-bromo-5-methoxyphenyl; 3-bromophenyl; 3-bromophenylmethyl; 3-carboxamidophenyl; 3-chlorophenyl; 3-cyanophenyl; 3-diethylmalonylallylphenyl; 3-10 dimethylaminophenyl; 3-ethoxyphenyl; 3-fluoro-5-trifluoromethylphenyl; 3-fluorophenyl; 3-hydroxyphenyl; 3-iodophenyl; 3-methoxyethoxyphenyl; 3-methoxyphenyl; 3-methylphenyl; 3-methylsulfonylphenyl; 3-methylthiophenyl; 3-t-butylacrylphenyl; 3-trifluoromethoxyphenyl; 3-trifluoromethylphenyl; 3-vinylpyridinylphenyl; 3,4,5-dichlorophenyl; 3,4-dimethoxyphenyl; 3,4-methylenedioxyphenyl; 3,4,5-15 trimethoxyphenyl; 3,5-di(trifluoromethyl)phenyl; 3,5-dibromophenyl; 3,5-dichlorophenyl; 3,5-dimethoxyphenyl; 3,5-dimethylphenyl; 4-(2-propyl)phenyl; 4-(2-propyl)oxyphenyl; 4-benzylxyphenyl; 4-bromophenyl; 4-bromothiophene-2-yl; 4-butoxyphenyl; 4-dimethylaminophenyl; 4-fluoro-3-trifluoromethylphenyl; 4-methoxyphenyl; 4-neopentylphenyl; 4-phenoxyphenyl; 5-bromothiophene-2-yl; 5-cyclohexyl; 5-cyclopropyl; 20 5-hexyl; 5-methyl; 5-phenyl; (2-bromo-5-chlorophenyl)methyl; (2-bromophenyl)methyl; (5-chloro-2-(3-methoxyphenyl)phenyl)methyl; 3-bromophenyl; 2-pyridyl; 2-ethoxyphenyl; 5-ethoxyphenyl; 2,5-dichlorophenyl; 2,5-dimethylphenyl; 3-fluorophenyl; 3-trifluoromethylphenyl; 5-trifluoromethylphenyl; 3,5-diclorophenyl; 4-bromo-2-thienyl; 3-bromo-2-thienyl; 3-cyanophenyl; 4-tetrahydropyranyl; 3-indolyl; 5-indolyl; 4-quinolyl; 25 2-bromophenyl; 4-fluorophenyl; 4,4-disfluorocyclohexyl; 1,1-dimethyl-3-butenyl; 2,3-dichlorophenyl; isopropyl; and 2-trifluorophenylphenyl.

Exemplary and preferred adenosine kinase inhibitor compounds of the invention utilized in the method recited herein include the compounds listed below wherein R¹, R², R³, and R⁴ are as described in Formula I in the specific compound:

4-(N-(2,3-dihydroxypropyl)amino)-5-(3-bromophenyl)-7-(6-morpholinyl-3-pyridinyl)pyrido[2,3-d]pyrimidine,

4-(N-(3-morpholinylpropyl)amino)-5-(3-bromophenyl)-7-(6-morpholinyl-3-pyridinyl)pyrido[2,3-d]pyrimidine,

5 4-(N-(2-(4-imidazolyl)ethyl)amino)-5-(3-bromophenyl)-7-(6-morpholinyl-3-pyridinyl)pyrido[2,3-d]pyrimidine,

4-(N-(3-carboxypropyl)amino)-5-(3-bromophenyl)-7-(6-morpholinyl-3-pyridinyl)pyrido[2,3-d]pyrimidine,

10 (S)-4-amino-5-(3-bromophenyl)-7-(6-(O-methyl-2-hydroxymethylpyrrolidinyl)-3-pyridinyl)pyrido[2,3-d]pyrimidine,

(S)-4-amino-5-(3-bromophenyl)-7-(6-(2-hydroxymethylpyrrolidinyl)-3-pyridinyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(2-bromophenyl)-7-(6-(4-hydroxypiperidinyl)-3-pyridinyl)pyrido[2,3-d]pyrimidine,

15 4-amino-5-(4-fluorophenyl)-7-(6-(4,4-ethylenedioxypiperidinyl)-3-pyridinyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(2-bromophenyl)-7-(6-(4-hydroxypiperidinyl)-3-pyridazyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-(4,4-ethylenedioxypiperidinyl)-3-pyridazyl)pyrido[2,3-d]pyrimidine,

20 4-amino-5-(3-bromophenyl)-7-(2-morpholinyl-4-thiazolyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(N-methyl-3-indolyl)-7-(6-morpholinyl-3-pyridinyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-(4-ethoxyiminopiperidinyl)-3-pyridinyl)pyrido[2,3-d]pyrimidine,

25 4-amino-5-(3-bromophenyl)-7-(6-(4-ethoxycarbonylmethoxyiminopiperidinyl)-3-pyridinyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(4-dimethylaminophenyl)-7-(4-bromophenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(4-dimethylaminophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(4-methoxyphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine,

5 4-amino-5-(4-dimethylaminophenyl)-7-(4-methoxyphenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(4-(2-propyl)phenyl)-7-(4-methoxyphenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(4-neopentylphenyl)-7-(4-methoxyphenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(4-butyloxyphenyl)-7-(4-methoxyphenyl)pyrido[2,3-d]pyrimidine,

10 4-amino-5-(4-methoxyphenyl)-7-(4-bromophenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(4-(2-propyl)oxyphenyl)-7-(4-methoxyphenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(4-butoxyphenyl)-7-(4-N-formylpiperazinylphenyl)pyrido[2,3-d]pyrimidine,

15 4-amino-5-(4-benzyloxyphenyl)-7-(4-methoxyphenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(4-phenoxyphenyl)-7-(4-methoxyphenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(4-(2-propyl)phenyl)-7-(4-diethylmalonylallylphenyl)pyrido[2,3-d]pyrimidine,

20 4-amino-5-(4-(2-propyl)phenyl)-7-(4-t-butylacylphenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3,4-dimethoxyphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine,

25 4-amino-5-(3-t-butylacrylphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-methoxyphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3,5-dimethoxyphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine,

30 4-amino-5-(3-diethylmalonylallylphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-vinylpyridinylphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine.

4-amino-5-(3-trifluoromethylphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine.

4-amino-5-(3-carboxamidophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine,

5 4-amino-5-(3-cyanophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine.

4-amino-5-(3-benzyloxyphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine,

10 4-amino-5-(3-methoxyphenyl)-7-(4-methoxyphenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(4-butoxyphenyl)pyrido[2,3-d]pyrimidine,

10 4-amino-5-(3-(2-pyridyl)phenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-methylphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-chlorophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine,

15 4-amino-5-(3-fluorophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(4-methoxyphenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-methoxyphenyl)-7-(4-bromophenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-phenylpyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(4-ethylphenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(4-bromophenyl)pyrido[2,3-d]pyrimidine,

20 4-amino-5-(3-bromophenyl)-7-(4-cyanophenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(4-hydroxyphenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-iodophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-ethoxyphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-trifluoromethoxyphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine,

25 4-amino-5-(3,5-dichlorophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromo-4-fluorophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine,

30 4-amino-5-(3-hydroxyphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(4-morpholinylphenyl)pyrido[2,3-d]pyrimidine,
4-amino-5-(3-bromophenyl)-7-(4-piperidinylphenyl)pyrido[2,3-d]pyrimidine,
4-amino-5-(3-bromophenyl)-7-(4-(imidazol-1-yl)phenyl)pyrido[2,3-d]pyrimidine,
4-amino-5-(3-bromophenyl)-7-(4-chlorophenyl)pyrido[2,3-d]pyrimidine,
5 4-amino-5-(3-bromophenyl)-7-(4-isopropylphenyl)pyrido[2,3-d]pyrimidine,
4-amino-5-(3-bromophenyl)-7-(4-trifluorophenyl)pyrido[2,3-d]pyrimidine,
4-amino-5-(3-bromophenyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine,
4-amino-5-(3-bromophenyl)-7-(3,4,5-trimethoxyphenyl)pyrido[2,3-d]pyrimidine,
4-amino-5-(3-(3-methoxybenzyl)phenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-
10 d]pyrimidine,
4-amino-5-(3-methoxyethoxyphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-
d]pyrimidine,
4-amino-5-(3,4-methylenedioxyphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-
d]pyrimidine,
15 4-amino-5-(3-bromophenyl)-7-(4-ethoxyphenyl)pyrido[2,3-d]pyrimidine,
4-amino-5-(3-bromophenyl)-7-(2'-thiophene)pyrido[2,3-d]pyrimidine,
4-amino-5-(3-bromophenyl)-7-(4-fluorophenyl)pyrido[2,3-d]pyrimidine,
4-amino-5-(3-dimethylaminophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-
d]pyrimidine,
20 4-amino-5-phenyl-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine,
4-amino-5-(3,4,5-trimethoxyphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-
d]pyrimidine,
4-amino-5-(3-bromophenyl)-7-(4-nitrophenyl)pyrido[2,3-d]pyrimidine,
25 4-amino-5-(3-bromophenyl)-7-(4-iodophenyl)pyrido[2,3-d]pyrimidine,
4-amino-5-(3-bromophenyl)-7-(3,4-methylenedioxyphenyl)pyrido[2,3-
d]pyrimidine,
4-amino-5-(thiophen-2-yl)-7-(4-morpholinylphenyl)pyrido [2,3-d]pyrimidine,
4-amino-5-(3,5-dimethoxyphenyl)-7-(thiophen-2-yle)pyrido [2,3-d]pyrimidine,
4-amino-5-(3-bromophenyl)-7-(4-carboxamidophenyl)pyrido[2,3-d]pyrimidine.

4-amino-5-(3-bromophenyl)-7-(4-(2-methoxyethoxyphenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3,5-dimethoxyphenyl)-7-(4-morpholinylphenyl)pyrido[2,3-d]pyrimidine,

5 4-amino-5-(3-trifluoromethylphenyl)-7-(thiophene-2-yl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(4-aminophenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromo-4-fluorophenyl)-7-(thiophene-2-yl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromo-4-fluorophenyl)-7-(2-furanyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3,5-dimethoxyphenyl)-7-(4-iodophenyl)pyrido[2,3-d]pyrimidine,

10 4-amino-5-(3,5-dimethoxyphenyl)-7-(4-imidazolylphenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3,5-dimethoxyphenyl)-7-(4-(thiophene-2-yl)phenyl)pyrido[2,3-d]pyrimidine,

15 4-amino-5-(3,5-dimethoxyphenyl)-7-(4-(3-pyridyl)phenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(4-(4-methylpiperidinyl)phenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(4-pyrrolidinylphenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(4-bromothiophene-2-yl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine,

20 4-amino-5-(4-bromothiophene-2-yl)-7-(4-morpholinylphenyl)pyrido[2,3-d]pyrimidine,

4-morpholinyl-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(5-bromothiophene-2-yl)-7-(4-morpholinylphenyl)pyrido[2,3-d]pyrimidine,

25 4-amino-5-(4-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(4-(acetylamino)phenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3,5-dimethoxyphenyl)-7-(5-pyrimidinylphenyl)pyrido[2,3-d]pyrimidine,

4-(4-fluorophenyl)amino)-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine.

4-amino-5-(4-bromothiophene-2-yl)-7-(4-pyrrolidinylphenyl)pyrido[2,3-d]pyrimidine,

5 4-amino-5-(4-bromothiophene-2-yl)-7-(thiophene-2-yl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(5-(dimethylamino)thiophene-2-yl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromo-5-iodophenyl)-7-(4-(dimethylamino)phenyl)pyrido[2,3-d]pyrimidine,

10 4-amino-5-(3,5-di(trifluoromethyl)phenyl)-7-(4-(dimethylamino)phenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3,5-di(trifluoromethyl)phenyl)-7-(4-morpholinylphenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3,5-dibromophenyl)-7-(4-(dimethylamino)phenyl)pyrido[2,3-d]pyrimidine,

15 4-amino-5-(3,5-dibromophenyl)-7-(4-morpholinylphenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(4-bromothiophene-2-yl)-7-(4-(4-methylpiperidinyl)phenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3,5-dibromophenyl)-7-(4-(dimethylamino)phenyl)pyrido[2,3-d]pyrimidine,

20 4-amino-5-(3-bromophenyl)-7-(3-(dimethylamino)phenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(4-methylsulfonylphenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(3-methoxyphenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(4-(methylthio)phenyl)pyrido[2,3-d]pyrimidine,

25 4-amino-5-(3-bromophenyl)-7-(3,4-dichlorophenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(4-(N-methyl-N-formylamino)phenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(4-methylaminophenyl)pyrido[2,3-d]pyrimidine,

30 4-amino-5-(3-bromo-4-fluorophenyl)-7-(4-methylsulfonylphenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(3-amino-4-methoxyphenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(3-bromo-4-(dimethylamino)phenyl)pyrido[2,3-d]pyrimidine,

5 4-amino-5-(3-bromophenyl)-7-(3-methyl-4-(dimethylamino)phenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(4-(N-methyl-N-trifluoroacetyl)amino)phenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(4-(dimethylamino)-3-fluorophenyl)pyrido[2,3-d]pyrimidine,

10 4-amino-5-(3-bromophenyl)-7-(4-(N-ethyl-N-formylamino)phenyl)pyrido[2,3-d]pyrimidine,

4,4-bis(acetylamino)-5-(3-bromophenyl)-7-(4-(N-methyl-N-acetyl)amino)phenyl)pyrido[2,3-d]pyrimidine,

15 4-amino-5-(3-bromophenyl)-7-(4-(N-acetyl-N-methylamino)phenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(4-(N-ethylamino)phenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(4-(N-methyl-N-(2-methoxyethyl)amino)phenyl)pyrido[2,3-d]pyrimidine,

20 4-amino-5-(3-bromophenyl)-7-(4-(N-isopropylamino)phenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(4-N-ethyl-N-(2-methoxyethyl)amino)phenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(4-N-(3-methoxypropionyl)-N-isopropylamino)phenyl)pyrido[2,3-d]pyrimidine,

25 4-amino-5-(3-bromophenyl)-7-(4-(N-(2-(dimethylamino)ethyl)-N-formylamino)phenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(4-(N-(2-(dimethylamino)ethyl)amino)phenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(4-(N-methyl-N-(2-cyanoethylamino)phenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(4-(N-methyl-N-(3-methoxy)propionylamino)phcnyl)pyrido[2,3-d]pyrimidine,

5 4-amino-5-(3-bromophenyl)-7-(3-methyl-4-(N-methylamino)phenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(3-methyl-4-(N-methylamino)phenyl)pyrido[2,3-d]pyrimidine,

10 4-amino-5-(3-bromophenyl)-7-(4-(4-methoxy-2-butyl)phenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(4-(N-methyl-N-(2-(N-phthalimidyl)acetyl)amino)phenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(3-methyl-4-(N-methyl-N-(trifluoroacetyl)amino)phenyl)pyrido[2,3-d]pyrimidine,

15 4-amino-5-(3-bromophenyl)-7-(3-methyl-4-(N-acetyl-N-methylamino)phenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-dimethylamino-3-pyridinyl)pyrido[2,3-d]pyrimidine,

20 4-amino-5-(3-cyanophenyl)-7-(4-methylsulfonylphenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-cyanophenyl)-7-(4-(N-methyl-N-formylamino)-phenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-(N-methyl-N-formylamino)-3-pyridinyl)pyrido[2,3-d]pyrimidine,

25 4-amino-5-(3-bromophenyl)-7-(6-morpholiny-3-pyridinyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-(N-methyl-N-methoxyethylamino)-3-pyridinyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-pyrrolidinyl-3-pyridinyl)pyrido[2,3-d]pyrimidine,

30 4-amino-5-(3-bromophenyl)-7-(2-(dimethylamino)-5-pyrimidinyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(2-(N-methoxyethyl-N-methyl amino)-5-pyrimidinyl)pyrido[2,3-d]pyrimidine.

4-amino-5-(3-bromophenyl)-7-(2-(N-formyl-N-methyl amino)-5-pyrimidinyl)pyrido[2,3-d]pyrimidine,

5 4-amino-5-(3-bromophenyl)-7-(2-(N-methylamino)5-pyrimidinyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(2-(1-pyrrolidinyl)-5-pyrimidinyl)pyrido[2,3-d]pyrimidine,

10 4-amino-5-(3-bromophenyl)-7-(2-(1-morpholinyl)-5-pyrimidinyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-(2-oxo-3-oxazolidinyl)-3-pyridinyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(2-pyridyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(3-pyridyl)pyrido[2,3-d]pyrimidine,

15 4-amino-5-(3-(thiophen-2-yl)phenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-(furan-2-yl)phenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine,

20 4-amino-5-(3-(3-methoxyphenyl)phenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-phenyl-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-chlorophenyl)-7-(4-(morpholinyl)phenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromo-4-fluorophenyl)-7-(4-(morpholinyl)phenyl)pyrido[2,3-d]pyrimidine,

25 4-amino-5-(3-chlorophenyl)-7-(4-iodophenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-chlorophenyl)-7-(4-(thiophen-2-yl)phenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-chlorophenyl)-7-(4-(5-pyrimidinyl)phenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromo-4-fluorophenyl)-7-(4-iodophenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(4-bromothiophene-2-yl)-7-(4-methoxyphenyl)pyrido[2,3-d]pyrimidine.

4-amino-5-(3-bromophenyl)methyl-7-(4-(dimethylamino)phenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(2-phenylethyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(2-methylpropyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine.

5 4-amino-5-(butyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine.

4-amino-5-(2-(4-bromophenyl)ethyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(butyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(2-(3-cyanophenyl)methyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine,

10 4-amino-5-(2-(N-phenylmethoxycarbonyl)aminoethyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(cycloheptyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(2-(5-chloro-2-(thiophen-3-yl)phenylmethyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine,

15 4-amino-5-(2-(3-bromophenyl)ethyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(pentyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-hexyl-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(2-(3-bromophenyl)ethyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine,

20 4-amino-5-((2-bromophenyl)methyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-cyclopropyl-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-cyclohexyl-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-((2-bromo-5-chlorophenyl)methyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine,

25 4-amino-5-methyl-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(2,3-methylenedioxyphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-fluoro-5-trifluoromethylphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine,

30 4-amino-5-(3-fluoro-5-trifluoromethylphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(2-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3,5-dimethylphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3,4-dichlorophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(4-fluoro-3-trifluoromethylphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromo-5-methoxyphenyl)-7-(4-morpholinylphenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromo-5-methoxyphenyl)-7-(4-pyrrolidinylphenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromo-5-methoxyphenyl)-7-(4-piperidinylphenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromo-5-methoxyphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-methylthiophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromo-5-methoxyphenyl)-7-(thiophene-2-yl)pyrido[2,3-d]pyrimidine,

4-amino-5-(2,3-dimethoxyphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-methylsulfonylphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine,

4-acetylamino-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine,

4-formylamino-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine,

4-(methoxycetyl)amino-5-(3-bromophenyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine,

4-trifluoroacetylamino-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine,

4-pentanoylamino-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine,

4-benzoylamino-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine,

5 4-(N-BOC-glycyl)amino-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine,

4-(N-phthalimidylglycyl)amino-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine,

10 4-(ethoxycarbonyl)amino-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine,

4-(ethylaminocarbonyl)amino-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine,

15 4-allylamino-5-(3-bromophenyl)-7-(4-dimethylaminophenyl) pyrido[2,3-d]pyrimidine,

4-(2-(N,N-dimethylamino)ethylamino)-5-(4-bromophenyl)-7-(4-dimethylaminophenyl) pyrido[2,3-d]pyrimidine,

4-(4-(N,N-dimethylamino)butylamino)-5-(3-bromophenyl)-7-(4-dimethylaminophenyl) pyrido[2,3-d]pyrimidine,

20 4-(N-allyl-N-formylamino)-5-(4-dimethylaminophenyl)-7-(4-bromophenyl)pyrido[2,3-d]pyrimidine,

4-diacetylamino-5-(p-dimethylaminophenyl)-7-(4-bromophenyl)pyrido[2,3-d]pyrimidine,

25 pyridyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(5-amino-2-pyridyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(5-dimethylamino-2-pyrazinyl)pyrido[2,3-d]pyrimidine,

30 4-amino-5-(3-bromophenyl)-7-(2-oxobenzoxazolin-6-yl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(1-methyl-2-oxobenzoxazolin-6-yl)pyrido[2,3-d]pyrimidine,

4-amino-5-((5-chloro-2-(3-methoxyphenyl)phenyl)methyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-((thiophene-2-yl)methyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine,

5 4-amino-5-((thiophene-3-yl)methyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-((2-bromophenyl)methyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine,

10 4-amino-5-(3-bromophenyl)-7-(4-(N-formyl-N-(2-methoxyethyl)amino)phenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(4-(N-(2-methoxyethyl)amino)phenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(4-(N-methyl-N-(2-dimethylamino)ethyl)amino)phenyl)pyrido[2,3-d]pyrimidine,

15 4-amino-5-(3-bromophenyl)-7-(4-(2-methoxy)acetyl)amino)ethyl)amino)phenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-((4-formylamino)phenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(4-(2-(dimethylamino)acetyl)amino)phenyl)pyrido[2,3-d]pyrimidine,

20 4-amino-5-(3-bromophenyl)-7-(4-(2-oxo-3-oxazolidinyl)phenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-(2-propyl)-3-pyridinyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(3-methyl-4-pyrrolidinylphenyl)pyrido[2,3-d]pyrimidine,

25 4-amino-5-(3-bromophenyl)-7-(6-imidazolyl-3-pyridinyl)pyrido[2,3-d]pyrimidine,

4-amino-5-phenylmethyl-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(2-(3-aminopropynyl)phenylmethyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine,

30 4-amino-5-(1-(3-bromophenyl)ethyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(4-dimethylaminophenyl)-7-(4-bromophenyl)pyrido[2,3-d]pyrimidine,
4-amino-5-(2-furanyl)-7-(4-(N-morpholinyl)phenyl)pyrido[2,3-d]pyrimidine,
4-amino-5-(3-bromophenyl)-7-(2-dimethylamino-5-pyrimidinyl)pyrido[2,3-d]pyrimidine,
5 4-amino-5-(3-bromophenyl)-7-(4-(ureido)phenyl)pyrido[2,3-d]pyrimidine,
4-amino-5-(1-phenylmethyl-3-piperidinyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine,
4-amino-5-(3-bromophenyl)-7-(6-(3-methyl-5-isoxazolyl))-3-pyridinyl)pyrido[2,3-d]pyrimidine,
10 4-amino-5-(3-bromophenyl)-7-(6-chloro-3-pyridinyl)pyrido[2,3-d]pyrimidine,
4-amino-5-(3-bromophenyl)-7-(6-methoxy-3-pyridinyl)pyrido[2,3-d]pyrimidine,
4-amino-5-(3-bromophenyl)-7-(6-(1,2,4-triazol-4-yl)-3-pyridinyl)pyrido[2,3-d]pyrimidine,
15 4-amino-5-(3-bromophenyl)-7-(2-morpholinyl-5-pyrimidinyl)pyrido[2,3-d]pyrimidine,
4-amino-5-(2-thiazolyl)-7-(4-pyrrolidinylphenyl)-pyrido[2,3-d]pyrimidine,
4-amino-5-(3-bromophenyl)-7-(6-pyrazolyl-3-pyridinyl)-pyrido[2,3-d]pyrimidine,
20 4-amino-5-(3-bromophenyl)-7-(4-(1-methyl-ureido)phenyl)-pyrido[2,3-d]pyrimidine,
4-amino-5-(3-bromophenyl)-7-(4-(N-methyl-N-(2-pyrimidinyl)amino)phenyl)-pyrido[2,3-d]pyrimidine,
4-amino-5-(3-bromophenyl)-7-(3-fluoro-4-(N-formyl-N-methylamino)phenyl)-pyrido[2,3-d]pyrimidine,
25 4-formylamino-5-(3-bromophenyl)-7-(3-fluoro-4-(N-formyl-N-methylamino)phenyl)-pyrido[2,3-d]pyrimidine,
4-amino-5-(3-bromophenyl)-7-(4-(N-methyl-N-methylsulfonylamino)phenyl)-pyrido[2,3-d]pyrimidine.

4-amino-5-(3-bromophenyl)-7-(6-(N-methyl-N-methylsulfonylamino)-3-pyridinyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(1-methyl-5-indolinyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(1-methyl-5-benzimidazolyl)pyrido[2,3-d]pyrimidine,

5 4-amino-5-(3-bromophenyl)-7-(6-dimethylamino-3-pyridazinyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3bromophenyl)-7-(6-morpholinyl-3-pyridazinyl)pyrido[2,3-d]pyrimidine,

10 4-amino-5-(3-bromophenyl)-7-(6-pyrrolidinyl-3-pyridazinyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(5-morpholinyl-2-pyrazinyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(5-(N-(2-methoxyethyl)-N-methylamino)-2-pyrazinyl)pyrido[2,3-d]pyrimidine,

15 4-amino-5-(3-bromophenyl)-7-(4-(morpholinylmethyl)-phenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(5-(N,N-bis(2-methoxyethyl)amino)-2-pyridinyl)pyrido[2,3-d]pyrimidine,

20 4-amino-5-(3-bromophenyl)-7-(4-(imidazolylmethyl)-phenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(5-(1-morpholinyl)-2-pyridinyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(4-((dimethylamino)methyl)-phenyl)pyrido[2,3-d]pyrimidine,

25 4-amino-5-(3-bromophenyl)-7-(5-(4-hydroxy-1-piperidinyl)-2-pyridinyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(5-(N-formyl-N-methylamino)-2-pyridinyl)pyrido[2,3-d]pyrimidine.

4-amino-5-(3-bromophenyl)-7-(5-(2-propenyl)-2-pyridinyl)pyrido[2,3-d]pyrimidine.

4-amino-5-(3-bromophenyl)-7-(3-(2-methoxyethyl)-2-oxo-6-benzoxazolyl)pyrido[2,3-d]pyrimidine,

5 4-amino-5-(3-bromophenyl)-7-(4-(1-(N-formylamino)-ethyl)phenyl)pyrido[2,3-d]pyrimidine,

4-(methylamino)-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine hydrochloride;

4-(2-methoxyethylamino)-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine hydrochloride;

10 4-amino-5-(3-bromophenyl)-7-(4-(1-methyl-2-imidazolyl)phenyl)pyrido[2,3-d]pyrimidine trihydrochloride;

4-amino-5-(3-bromophenyl)-7-(4-(aminomethyl)phenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(2-bromo-4-(dimethylamino)phenyl)pyrido[2,3-d]pyrimidine,

15 4-amino-5-(3-bromophenyl)-7-(4-(dimethylaminoethyl)phenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(4-(3-(dimethylamino)propynyl)phenyl)pyrido[2,3-d]pyrimidine,

20 4-amino-5-(3-bromophenyl)-7-(4-(3-amino-3-methylbutynyl)phenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(4-dimethylphosphonatophenyl)pyrido[2,3-d]pyrimidine,

25 4-amino-5-(3-bromophenyl)-7-(4-(3-methoxypropynyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(4-carboxyphenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(4-methyl-3-oxo-2H-4H-pyrido[3,2-b]-1,4-oxazin-7-yl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(4-(2-(dimethylamino)ethyl)-3-oxo-2H-4H-pyrido[3,2-b]-1,4-oxazin-7-yl)pyrido[2,3-d]pyrimidine.

4-amino-5-(3-bromophenyl)-7-(2,3-dihydro-3-(dimethylaminoethyl)-2-oxobenzoxazol-6-yl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(4-methyl-3-oxo-2H-4H-benzo-1,4-oxazin-7-yl)pyrido[2,3-d]pyrimidine,

5 4-amino-5-(3-bromophenyl)-7-(2,2,4-trimethyl-3-oxo-2H-4H-benzo-1,4-oxazin-7-yl)pyrido[2,3-d]pyrimidine,

4-amino-5-cyclohexyl-7-(4-(2-dimethylamino)ethyl)-2H-4H-benzo-3-oxo-1,4-oxazin-7-yl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(5-(1-methylethyl)-2-pyridyl)pyrido[2,3-10 d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(5-piperidin-1-ylpyrid-2-yl)pyrido[2,3-d]pyrimidine,

4-amino-5-(1-(4-bromophenyl)ethyl)-7-(6-morpholinylpyrid-3-yl)pyrido[2,3-d]pyrimidine,

15 4-amino-5-(3-bromophenyl)-7-(4-((N-formylamino)methyl)phenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(4-(1-methyl-1-(N-methylamino)ethyl)phenyl)-pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(4-(1-dimethylamino)-1-20 methylethyl)phenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(N-acetyl-5-indolinyl)pyrido[2,3-d]pyrimidine,

4-amino-5-cyclohexyl-7-(6-chloro-3-pyridyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(1-(2-bromophenyl)ethyl)-7-(6-diethylamino-3-pyridyl)pyrido[2,3-25 d]pyrimidine,

4-amino-5-(1-(2-bromophenyl)ethyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(1-(2-bromophenyl)ethyl)-7-(4-(N-methyl-N-formyl)amino)-phenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-cyclohexyl-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine.

4-amino-5-((2-bromophenyl)methyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(4-tetrahydropyranyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine,

5 4-amino-5-cyclohexyl-7-(6-dimethylamino-3-pyridyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(1-ethylpropyl)-7-(6-dimethylamino-3-pyridyl)pyrido[2,3-d]pyrimidine,

4-amino-5-cyclopentyl-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine,

4-amino-5-cyclohexyl-7-(2-chloro-3-pyridyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3,5-dimethylcyclohexyl)-7-(6-dimethylamino-3-pyridyl)pyrido[2,3-d]pyrimidine,

10 4-amino-5-((N-(benzyloxycarbonyl)-4-piperidinyl)methyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine,

4-amino-5-cyclohexyl-7-(6-bromo-3-pyridyl)pyrido[2,3-d]pyrimidine,

4-amino-5-cyclohexyl-7-(3-cyanophenyl)pyrido[2,3-d]pyrimidine,

15 4-amino-5-(1-(2-bromophenyl)ethyl)-7-(6-dimethylamino-3-pyridazinyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-imidazolyl-3-pyridazinyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-(azacycloheptanyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine,

20 4-amino-5-(3-bromophenyl)-7-(6-(N-methyl-N-(1-methylethyl))amino)-3-pyridazinyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(1-(2-bromophenyl)ethyl)-7-(6-morpholinyl-3-pyridazinyl)pyrido[2,3-d]pyrimidine,

25 4-amino-5-cyclohexyl-7-(6-(4-acetyl(piperazinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine,

4-amino-5-cyclohexyl-7-(6-(4-acetyl-1,4-diazacycloheptanyl)-3-pyridyl)pyrido[2,3-d]pyrimidine,

4-amino-5-cyclohexyl-7-(6-(4-methyl-1,4-diazacycloheptanyl)-3-pyridyl)pyrido[2,3-d]pyrimidine,

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4-amino-5-cyclohexyl-7-(6-(N-methyl-N-(2-(2-pyridyl)ethyl)amino)-3-pyridyl)pyrido[2,3-d]pyrimidine,

4-amino-5-cyclohexyl-7-(6-2-(N-(N',N'-dimethylaminoethyl)-N-methylamino)-3-pyridyl)pyrido[2,3-d]pyrimidine,

5 4-amino-5-cyclohexyl-7-(6-azetidinyl-3-pyridyl)pyrido[2,3-d]pyrimidine,

4-amino-5-cyclohexyl-7-(6-(3-(N-methylacetamido)pyrrolidinyl)pyridyl)pyrido[2,3-d]pyrimidine,

4-amino-5-cyclohexyl-7-(6-(3-(formamido)pyrrolidinyl)pyridyl)pyrido[2,3-d]pyrimidine,

10 4-amino-5-cyclohexyl-7-(4-oxo-1-phenyl-1,3,8-triazaspiro[4.5[decan-8-yl]pyrido[2,3-d]pyrimidine,

4-amino-5-cyclohexyl-7-(6-(2-methoxymethyl)pyrrolidin-1-yl)pyridyl)pyrido[2,3-d]pyrimidine,

4-amino-5-cyclohexyl-7-(6-(N-methoxyethyl-N-propylamino)pyridyl)pyrido[2,3-d]pyrimidine,

15 4-amino-5-cyclohexyl-7-(N-methyl-N-(2,2-dimethoxyethyl)amino)pyrido[2,3-d]pyrimidine,

4-amino-5-cyclohexyl-7-(6-(4-(dimethylamino)piperidinyl)pyridyl)pyrido[2,3-d]pyrimidine,

20 4-amino-5-cyclohexyl-7-(6-(4-(aminocarbonyl))piperidinyl)pyridyl)pyrido[2,3-d]pyrimidine,

4-amino-5-cyclohexyl-7-(N-methyl-N-(3-(diethylamino)propyl)aminopyrid-3-yl)pyrido[2,3-d]pyrimidine,

4-amino-5-cyclohexyl-7-(6-(N-methyl-N-(4-pyridyl)ethylamino)pyrid-3-yl)pyrido[2,3-d]pyrimidine,

25 4-amino-5-cyclohexyl-7-(6-(N-methyl-N-(3-pyridylmethylamino)pyrid-3-yl)pyrido[2,3-d]pyrimidine,

4-amino-5-(1-(2-bromophenyl)ethyl)-7-(1-methyl-5-indolyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(1-(2-bromophenyl)ethyl)-7-(1-methyl-2,3-dioxo-5-indolyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(3-fluoro-4-(1-morpholinyl)phenyl)pyrido[2,3-d]pyrimidine,

5 4-amino-5-(3-bromophenyl)-7-(4-hydroxy-3-nitrophenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-(4,4-ethylenedioxypiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-(4-oxopiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine,

10 4-amino-5-(3-bromophenyl)-7-(6-(4-formylpiperazinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-(4-methylpiperazinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-thiomorpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidin;

15 4-amino-5-(3-bromophenyl)-7-(6-(4,4-dioxothiomorpholinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(2-bromophenyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromo-4-methoxyphenyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine,

20 4-amino-5-(4-bromophenyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-chlorophenyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(5-chloro-6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine,

25 4-amino-5-(3-bromophenyl)-7-(6-(N-oxidomorpholinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-(N-(2-hydroxyethoxyethyl)amino)-3-pyridyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-(N-(2-hydroxyethoxyethyl)-N-formylamino)-3-pyridyl)pyrido[2,3-d]pyrimidine.

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4-amino-5-(3-bromophenyl)-7-(6-(N-(2-hydroxyethoxyethyl)-3-pyridyl-N-oxide)pyrido[2,3-d]pyrimidine.

4-amino-5-(3-bromophenyl)-7-(6-(3-hydroxy)morpholinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine.

5 1-(5-(4-amino-5-(3-bromophenyl)pyrido[2,3-d]pyrimidin-7-yl)-2-pyridyl)-piperidine-4-phosphate, disodium salt;

4-amino-5-(3-bromophenyl)-7-(4-methylenylpiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine,

10 4-amino-5-(3-bromophenyl)-7-(4-hydroxy-4-(hydroxymethyl)piperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-(4,4-ethylenedioxypiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine.

4-amino-5-cyclohexyl-7-(6-(4-oxo-piperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine,

15 4-amino-5-cyclohexyl-7-(6-(4-methylenylpiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine,

4-N-(iminomethyl)amino-5-cyclohexyl-7-(6-dimethylamino-3-pyridyl)pyrido[2,3-d]pyrimidine,

4-allylamino-5-(4-bromophenyl)-7-(4-dimethylaminophenyl) pyrido[2,3-d]pyrimidine,

20 4-amino-5-(3-bromophenyl)-7-(6-(4-hydroxypiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(cyclohexyl)-7-(6-(4,4-ethylenedioxypiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine,

25 4-amino-5-(3-bromophenyl)-7-(2-morpholinyl-5-thiazolyl)pyrido[2,3-d]pyrimidine,

4-(N-(2,3-dihydroxypropyl)amino)-5-(3-bromophenyl)-7-(6-morpholinyl-3-pyridinyl)pyrido[2,3-d]pyrimidine,

4-(N-(3-morpholinylpropyl)amino)-5-(3-bromophenyl)-7-(6-morpholinyl-3-pyridinyl)pyrido[2,3-d]pyrimidine.

4-(N-(2-(4-imidazolyl)ethyl)amino)-5-(3-bromophenyl)-7-(6-morpholinyl-3-pyridinyl)pyrido[2,3-d]pyrimidine,

4-(N-(3-carboxypropyl)amino)-5-(3-bromophenyl)-7-(6-morpholinyl-3-pyridinyl)pyrido[2,3-d]pyrimidine.

5 (S)-4-amino-5-(3-bromophenyl)-7-(6-(O-methyl-2-hydroxymethylpyrrolidinyl)-3-pyridinyl)pyrido[2,3-d]pyrimidine,

(S)-4-amino-5-(3-bromophenyl)-7-(6-(2-hydroxymethylpyrrolidinyl)-3-pyridinyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(2-bromophenyl)-7-(6-(4-hydroxypiperidinyl)-3-pyridinyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(4-fluorophenyl)-7-(6-(4,4-ethylenedioxypiperidinyl)-3-pyridinyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(2-bromophenyl)-7-(6-(4-hydroxypiperidinyl)-3-pyridazyl)pyrido[2,3-d]pyrimidine,

15 4-amino-5-(3-bromophenyl)-7-(6-(4,4-ethylenedioxypiperidinyl)-3-pyridazyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(2-morpholinyl-4-thiazolyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(N-methyl-3-indolyl)-7-(6-morpholinyl-3-pyridinyl)pyrido[2,3-d]pyrimidine,

20 4-amino-5-(3-bromophenyl)-7-(6-(4-ethoxyiminopiperidinyl)-3-pyridinyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-(4-ethoxycarbonylmethoxyiminopiperidinyl)-3-pyridinyl)pyrido[2,3-d]pyrimidine,

25 4-amino-5-(3-bromophenyl)-7-(6-(4-oxopiperidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-(4-morpholinyliminopiperidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptan-5-yl)-3-pyridazyl)pyrido[2,3-d]pyrimidine.

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4-amino-5-(3-bromophenyl)-7-(6-(4-methoxyiminopiperidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-phenylmethoxy-3-pyridazinyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-(4-methoxypiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine,

5 4-amino-5-(3-bromophenyl)-7-(6-(4-tetrahydropyranloxy)iminopiperidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-isobutoxy-3-pyridazinyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-(4-(N-methylpiperazinyl)iminopiperidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine,

10 4-amino-5-(3-bromophenyl)-7-(6-(4-ethoxypiperidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-(4-tetrahydropyranloxy)-3-pyridazinyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-morpholylethoxy-3-pyridazinyl)pyrido[2,3-d]pyrimidine,

15 4-amino-5-(3-bromophenyl)-7-(6-(4-ethoxypiperidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-(4-(2-ethoxyethoxy)piperidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-(4-(4-tetrapyranyloxyethyl)piperidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine,

20 4-amino-5-(3-bromophenyl)-7-(6-(3-(R)-tetrahydrofuranloxy)piperidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-(3-(S)-tetrahydrofuranloxy)piperidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine,

25 4-amino-5-(3-bromophenyl)-7-(6-(trans-3-ethoxy-4-hydroxy)pyrrolidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-(cis-3-ethoxy-4-hydroxy)pyrrolidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-(trans-3-ethoxy-4-hydroxy)pyrrolidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine,

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4-amino-5-(3-bromophenyl)-7-(6-(trans-3,4-bis-ethoxy)pyrrolidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine.

4-amino-5-(3-bromophenyl)-7-(6-(trans-3,4-bis-ethoxy)pyrrolidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine,

5 4-amino-5-(3-bromophenyl)-7-(6-(cis-3,4-bis-ethoxy)pyrrolidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-(cis-3,4-bis-ethoxy)pyrrolidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-(cis-3-ethoxy-4-hydroxy)pyrrolidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine,

10 4-amino-5-(3-bromophenyl)-7-(6-(cis-3-amino-4-hydroxy)pyrrolidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-(cis-3-amino-4-hydroxy)pyrrolidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine,

15 4-amino-5-(2-pyridyl)-7-(6-(1,4-dioxa-8-azaspiro[4.5]decan-8-yl)-3-pyridyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(2,3-dichlorophenyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(2-pyridyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(2-ethoxyphenyl)-7-(6-(1,4-dioxa-8-azaspiro[4.5]decan-8-yl)-3-pyridyl)pyrido[2,3-d]pyrimidine,

20 4-amino-5-(2-bromo-5-ethoxyphenyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(2,5-dichlorophenyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(2,5-dimethylphenyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine

25 4-amino-5-(3-fluorophenyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-trifluoromethylphenyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-fluoro-5-trifluoromethylphenyl)-7-(6-(1,4-dioxa-8-azaspiro[4.5]decan-8-yl)-3-pyridyl)pyrido[2,3-d]pyrimidine.

4-amino-5-(3,5-diclorophenyl)-7-(6-(1,4-dioxa-8-azaspiro[4.5]decan-8-yl)-3-pyridyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-(1,5-dioxa-9-azaspiro[5.5]undecan-9-yl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine,

5 4-amino-5-(4-bromo-2-thienyl)-7-(6-(1,4-dioxa-8-azaspiro[4.5]decan-8-yl)-3-pyridyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-(4-tertbutyl)piperidinyl-3-pyridazinyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-(4-N-formyl)piperidinyl-3-pyridazinyl)pyrido[2,3-d]pyrimidine,

10 4-amino-5-(3-bromophenyl)-7-(6-(4,4-ethylenedioxypiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-cyanophenyl)-7-(6-morpholinyl-3-pyridazinyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-Bromophenyl)-7-(6-(S-O-ethyl-2-hydroxymethylpyrrolidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine,

15 4-amino-5-(3-bromophenyl)-7-(6-((2S,3S)-2,3-dimethyl-1,4-dioxa-8-azaspiro[4.5]decan-8-yl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-(4,4-(cis-1,2-dioxycyclopentyl)piperidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine,

20 4-amino-5-(3-bromophenyl)-7-(6-(4-acetyl-1-oxa-4,8-diazaspiro[4.5]decan-8-yl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-((2R,3R)-2,3-bis(methoxymethyl)-1,4-dioxa-8-azaspiro[4.5]decan-8-yl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine,

25 4-amino-5-(3-bromophenyl)-7-(6-(4,4-(cis-3,4-dioxy-oxacyclopentyl)piperidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-(3-methoxy-1,5-dioxa-9-azaspiro[5.5]undecan-9-yl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-(1,5-dioxa-3-hydroxymethyl-9-azaspiro[5.5]undecan-9-yl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine,

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4-amino-5-(3-bromophenyl)-7-(6-(1,7,14-trioxa-11-azadispiro[4.2.5.2]pentadecan-11-yl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(4-tetrahydropyranyl)-7-(6-morpholinyl-3-pyridazinyl)pyrido[2,3-d]pyrimidine,

5 4-amino-5-(3-bromophenyl)-7-(6-(4-morpholinylminopiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-(4-(N-methylpiperazinyl)iminopiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-(4-(1,2,4-triazol-1-yl)iminopiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine,

10 4-amino-5-(3-indolyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(5-indolyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-(4-ethylpiperidinylcarboxylate)-3-pyridyl)pyrido[2,3-d]pyrimidine,

15 4-amino-5-(3-bromophenyl)-7-(2-phenylmethyl-3(2H)-pyridazinone-6-yl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-(4-(morpholinylcarboxamide)piperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-(4-(N-morpholinylaminocarboxamide)piperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine,

20 4-amino-5-(3-bromophenyl)-7-(6-(4-(N,N-dimethylaminocarboxamide)piperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-(4-(N-methoxyethylcarboxamide)piperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(4-quinolyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine,

25 4-amino-5-(3-bromophenyl)-7-(6-(4-(N-methoxyethylcarboxamide)piperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-(4-hydroxymethylpiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(2-bromophenyl)-7-(6-(1,4-dioxa-8-azaspiro[4.5]decan-8-yl)-3-pyridyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(2-bromophenyl)-7-(6-(4-hydroxypiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine,

5 4-amino-5-(3-bromophenyl)-7-(6-(4-N-acetyl piperazinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-(4-cyanopiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-(4-N-(4-fluorophenyl)piperazinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine,

10 4-amino-5-(4-fluorophenyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(4-morpholinylbenzenesulfonamide)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(4-N-1,4-dioxa-8-azaspiro[4.5]decan-8-ylbenzenesulfonamide)pyrido[2,3-d]pyrimidine,

15 4-amino-5-(3-bromophenyl)-7-(4-N-cyclopropylbenzenesulfonamide)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(4-piperidinebenzenesulfonamide)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(4-(4-cyanopiperidine)benzenesulfonamide)pyrido[2,3-d]pyrimidine,

20 4-amino-5-(3-bromophenyl)-7-(4-N-cyclopropylmethylbenzenesulfonamide)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(4-N,N-dimethylaminobenzenesulfonamide)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(4-N-(S)-2-

25 hydroxymethylpyrrolidinebenzenesulfonamide)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(4-(4-hydroxypiperidine)benzenesulfonamide)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(4-(*cis*-3,5-

dimethylmorpholinyl)benzenesulfonamide)pyrido[2,3-d]pyrimidine.

4-amino-5-(3-bromophenyl)-7-(3-fluoro-4-thiomorpholinylphenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(4-fluorophenyl)-7-(6-(thiomorpholinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(4-fluorophenyl)-7-(6-(4,4-dioxothiomorpholinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine,

5 4-amino-5-(3-bromophenyl)-7-(4-(4-dioxa-8-azaspiro[4.5]decan-8-ylcarboxamide)phenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(4-(N-cyclopropylcarboxamide)phenyl)pyrido[2,3-d]pyrimidine,

10 4-amino-5-(3-bromophenyl)-7-(4-(morpholinylcarboxamide)phenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-N-cyclopropylamino-3-pyridyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(4-(4-hydroxypiperidinylcarboxamide)phenyl)pyrido[2,3-d]pyrimidine,

15 4-amino-5-(3-bromophenyl)-7-(6-(S)-hydroxymethylpyrrolidinyl-3-pyridazinyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-(4-(2-ethoxyethoxy)piperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine,

20 4-amino-5-(3-bromophenyl)-7-(6-hexahydropyrimidine-3-pyridyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(4,4-difluorocyclohexyl)-7-(6-(1,4-dioxa-8-azaspiro[4.5]decan-8-yl)-3-pyridyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-(S)-2-ethoxyethoxypyrrolidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine,

25 4-amino-5-(3-bromophenyl)-7-(6-(R)-2-ethoxyethoxypyrrolidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-(cis-3,4-dihydroxypyrolidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-((3aR,6aS)-2-oxo-tetrahydro-3aH-[1.3]dioxolo[4.5-c]pyrrol-5-yl)-3-pyridyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-(cis-2,3-dihydroxypyrrolidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine,

5 4-amino-5-(3-bromophenyl)-7-(6-(S,R-2-hydroxymethyl-4-hydroxypyrrolidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-(R-2-hydroxymethyl-4-pyrrolidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptan-5-yl)-3-pyridyl)pyrido[2,3-d]pyrimidine,

10 4-amino-5-(3-bromophenyl)-7-(6-(2-imidizolidone-1-yl)-3-pyridyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(1,1-dimethyl-3-butenyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-(2,4-dioxo-(1H,3H)-quinazolin-3-yl)-3-pyridyl)pyrido[2,3-d]pyrimidine,

15 4-amino-5-(3-bromophenyl)-7-(6-carboxamide-3-pyridazinyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-morpholinylcarboxamide-3-pyridazinyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-methoxy-3-pyridazinyl)pyrido[2,3-d]pyrimidine,

20 4-amino-5-(3-bromophenyl)-7-(6-N,N-diethoxyethylamino-3-pyridazinyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-(4-ethoxymethylpiperidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-(4-(4-tetrahydropyranoxymethyl)piperidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine,

25 4-amino-5-(3-bromophenyl)-7-(6-(4-ethoxyethoxymethylpiperidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-(4-ethoxyethoxymethylpiperidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-N-methyl-N-1,3-dioxalanemethylamino)-3-pyridazinyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-(1,4-dioxaspiro[4.5]decanyl-8-oxy)-3-pyridazinyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-dihydroxymethylmethoxy-3-pyridazinyl)pyrido[2,3-d]pyrimidine,

5 4-amino-5-(3-bromophenyl)-7-(6-(3-pyridyloxy)-3-pyridazinyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-(4,7-epoxy-7-methyl-2,3,3A,4,5,6,7,7a-octahydro-1H-isoindolyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-(4-N-ethyl-N-methoxyethyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine,

10 4-amino-5-(3-bromophenyl)-7-(6-(4-N-methyl-N-methoxyethyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-(3,4-dimethoxymethoxy-pyrrolidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-(hexahydro-1H-furo[3,4-c]pyrrol-5-yl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine,

15 4-amino-5-(3-bromophenyl)-7-(6-(hexahydro-1H-furo[3,4-c]pyrrol-5-yl)-3-pyridyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-(trans-3-hydroxy-4-methylpyrrolidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine,

20 4-amino-5-(3-bromophenyl)-7-(6-(trans-3-hydroxy-4-methylpyrrolidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-(cis-3-hydroxy-4-methylpyrrolidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-(cis-3-hydroxy-4-methylpyrrolidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine,

25 4-amino-5-(3-bromophenyl)-7-(6-(trans-3-cyano-4-hydroxylpyrrolidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-(3-hydroxy-4-tert-butylcarboxamide-pyrrolidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-(S-2-(4-tetrahydropyranloxy)methylpyrrolidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-(3-(4-tetrahydropyranloxy)iminopyrrolidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine,

5 4-amino-5-(3-bromophenyl)-7-(2-morpholinyl-5-thiazoyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(5-bromo-2-thienyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(2,5-dimethyl-3-thienyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(5-chloro-2-thienyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(2,4-dimethyl-5-thiazoyl)pyrido[2,3-d]pyrimidine,

10 4-amino-5-(3-bromophenyl)-7-(5-methyl-2-thienyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(2-furanyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(2-(1,4-dioxa-8-azaspiro[4.5]decan-8-yl)-5-thiazoyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(3-thienyl)pyrido[2,3-d]pyrimidine,

15 4-amino-5-(3-bromophenyl)-7-(3-methyl-2-thienyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(2-morpholinyl-4-thiazoyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(2-morpholinyl-4-trifluoromethyl-5-thiazoyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(5-morpholinyl-2-thienyl)pyrido[2,3-d]pyrimidine,

20 4-amino-5-(3-bromophenyl)-7-(4-methyl-2-morpholinyl-5-thiazoyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(2,5-dichloro-3-thienyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(2,5-dimethyl-3-furanyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(N-methyl-2-pyrrolyl)pyrido[2,3-d]pyrimidine,

25 4-amino-5-(3-bromophenyl)-7-(2-N,N-dimethylamino-5-thiazoyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(2-morpholinyl-5-thiazoyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(2-(4,4-dioxythiomorpholiny)-5-thiazoyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(2-(1,1-dioxidothiomorpholiny)-5-thiazoyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(2-morpholiny-5-oxazolyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(2-N-methyl-N-methoxyethylamino-5-thiazoyl)pyrido[2,3-d]pyrimidine,

5 4-amino-5-(3-bromophenyl)-7-(2-N-methyl-N-ethylamino-5-thiazoyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(2-N-methyl-N-propylamino-5-thiazoyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(2-N-pyrrolidinyl-5-thiazoyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(2-(N-methylpiperazinyl)-5-thiazoyl)pyrido[2,3-d]pyrimidine,

10 4-amino-5-(3-bromophenyl)-7-(2-(N-(2-pyridyl)piperazinyl)-5-thiazoyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(2-N,N-diethylamino-5-thiazoyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(2-(N-methylpiperazinyl)-5-thiazoyl)pyrido[2,3-d]pyrimidine,

15 4-amino-5-(3-bromophenyl)-7-(2-(N-(2-pyridyl)piperazinyl)-5-thiazoyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(2-N-methy-N-(2-pyridylethyl)-5-thiazoyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(2-(4-oxopiperazinyl)-5-thiazoyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(2-(4-(N-morpholiny)iminopiperazinyl)-5-thiazoyl)pyrido[2,3-d]pyrimidine,

20 4-amino-5-(3-bromophenyl)-7-(2-(4-oxopiperidinyl)-5-pyrimidyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-N-morpholine-3-pyridinesulfonamide)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(2-(4-oxopiperidinyl)-5-pyrimidyl)pyrido[2,3-d]pyrimidine,

25 4-amino-5-(3-bromophenyl)-7-(2-(4,4-dioxethylenepiperidinyl)-5-pyrimidyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(5-(1,4-dioxa-8-azaspido[4.5]decan-8-yl)-2-pyrazinyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(5-(4-oxopiperidinyl)-2-pyrazinyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-N-cyclopropyl-3-pyridinesulfonamide)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-(N-1,4-dioxa-8-azaspiro[4.5]decan-8-yl)-3-pyridylsulfonamide)pyrido[2,3-d]pyrimidine,

5 4-amino-5-(3-bromophenyl)-7-(2-(4-(4-tetrahydropyranloxy)iminopiperidinyl)-5-pyrazinyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-(4-(phenylmethoxy)iminopiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-(4-(tert-butoxy)iminopiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine,

10 4-amino-5-(3-bromophenyl)-7-(6-(4-(cyclohexyloxy)iminopiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-(4-hydroxyiminopiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine,

15 4-amino-5-(3-bromophenyl)-7-(6-(4-(4-tetrahydropyranloxy)iminopiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-(4-methoxyethoxyiminopiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-(4-(2-thenylmethoxy)iminopiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine,

20 4-amino-5-(3-bromophenyl)-7-(6-(4-(4-(5'H-2-oxyfuranyl)-4-hydroxypiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-(4-(1-(4-tetrahydropyranloxy)iminoethyl))-4-hydroxypiperidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine,

25 4-amino-5-(3-bromophenyl)-7-(6-(4-(4'-acetyl-4'-hydroxypiperidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-(4-(1-(isopropylcaboxymethoxy)iminoethyl))-4-hydroxypiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-(4-(1-(ethylcaboxymethoxy)iminoethyl))-4-hydroxypiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine,

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4-amino-5-(3-bromophenyl)-7-(6-(4-(1-(methylcarboxymethoxy)iminoethyl))-4-hydroxypiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-(4-(1-(2-tetrahydropyranloxy)iminoethyl))-4-hydroxypiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine,

5 4-amino-5-(3-bromophenyl)-7-(6-(4-(1-(allyloxy)iminoethyl))-4-hydroxypiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-(4-(1-(ethoxy)iminoethyl))-4-hydroxypiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-(4-(1-(methoxy)iminoethyl))-4-hydroxypiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine,

10 4-amino-5-(3-bromophenyl)-7-(6-(4-(1-(hydroxy)iminoethyl))-4-hydroxypiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-(4-(2-tetrahydropyranloxy)iminopiperidinyl))-3-pyridyl)pyrido[2,3-d]pyrimidine,

15 4-amino-5-(3-bromophenyl)-7-(6-(4-(isopropylcarboxymethoxy)iminopiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-(4-hydroxy-4-(1-(4-tetrahydropyranloxy)iminoethyl))-4-hydroxypiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-(4-(3-butyrolactone)-4-hydroxypiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine,

20 4-amino-5-(3-bromophenyl)-7-(6-(4-(2-butyrolactone)-4-hydroxypiperidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-(4-acetyl-4-hydroxypiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine,

25 4-amino-5-(3-bromophenyl)-7-(6-(3-hydroxyazetidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-((1R,5S)-3-hydroxy-8-azabicyclo[3.2.1]octan-8-yl)-3-pyridyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-(cis-2,3-dihydroxypiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine,

30 4-amino-5-(3-bromophenyl)-7-(6-(cis-2,3-dihydroxypiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-(N-methyl-N-(3-pyridylmethyl)amino)-3-pyridazinyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-(1,2,3,6-tetrahydropyridyl)-3-pyridyl)pyrido[2,3-d]pyrimidine,

5 4-amino-5-(3-bromophenyl)-7-(6-(4-(N-4'methoxyphenylcarbamoyl)piperidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-(4-(2-butyrolactone)-4-hydroxypiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-(trans-3,4- bis(N-4'-methoxyphenylcarbamoyl)pyrrolidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine,

10 4-amino-5-(3-bromophenyl)-7-(6-((1S,5R)-3-hydroxy-8-azabicyclo[3.2.1]octan-8-yl)-3-pyridyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-(S,S-trans-3,4-dihydroxypyrrolidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine,

15 4-amino-5-(3-bromophenyl)-7-(6-(R,R-trans-3,4-dihydroxypyrrolidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-(R,R-trans-3,4-dihydroxypyrrolidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-(4-oxo-1-phenyl-1,3,8-triazaspiro[4.5]decan-8-yl)-3-pyridyl)pyrido[2,3-d]pyrimidine,

20 4-amino-5-(3-bromophenyl)-7-(6-(1-oxa-4-oxo-4-thia-8-azaspiro[4.5]decan-8-yl)-3-pyridyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-(1-oxa-4,4-dioxido-4-thia-8-azaspiro[4.5]decan-8-yl)-3-pyridyl)pyrido[2,3-d]pyrimidine,

25 4-amino-5-(3-bromophenyl)-7-(6-(4-oxo-1-phenyl-1,3,8-triazaspiro[4.5]dec-2-en-8-yl)-3-pyridyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-(4-(2-keto-1-benzimidazoliny)piperidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-(4-oxothiomorpholiny)-3-pyridyl)pyrido[2,3-d]pyrimidine,

30 4-amino-5-(3-bromophenyl)-7-(6-(4-oxothiomorpholiny)-3-pyridyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-(4-(2-keto-1-benzimidazoliny) piperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-(N-methyl-N-(2-pyridylethyl)amino)-3-pyridyl)pyrido[2,3-d]pyrimidine,

5 4-amino-5-(3-bromophenyl)-7-(6-(N-methyl-N-(4-pyridylethyl)amino)-3-pyridyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-N-(3-pyridylmethyl)amino-3-pyridyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-(2-hydroxymethylpiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine,

10 4-amino-5-(3-bromophenyl)-7-(6-(1-oxa-4-thia-8-azaspiro[4.5]decan-8-yl)-3-pyridyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-(4-hydroxy-4-(4-bromophenyl)piperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine,

15 4-amino-5-(3-bromophenyl)-7-(6-(4-N-(2-pyridinyl)piperazinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-(4-N-(2-hydroxyethoxyethyl)piperazinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-(4,4-diacetoxyethylthio)piperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine,

20 4-amino-5-(3-bromophenyl)-7-(6-(4-N-(2-pyridinyl)piperazinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-(N-methyl-N-(3-pyridylmethyl)amino)-3-pyridyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-(4-pyrrolidinylpiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine,

25 4-amino-5-(3-bromophenyl)-7-(6-(2-(1H-imidazol-4-yl)ethylamino)-3-pyridazinyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-(4-N-cyanomethylpiperazinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-(3-hydroxypyrroldinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine,

30 4-amino-5-(3-bromophenyl)-7-(6-(2-(1H-imidazol-4-yl)ethylamino)-3-pyridazinyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-(4-methylpiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-(cis-3,5-dimethylmorpholinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine,

5 4-amino-5-(3-bromophenyl)-7-(6-(4,4-difluoropipridinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-(1,1-dioxidothiomorpholinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-thiazolidinyl-3-pyridyl)pyrido[2,3-d]pyrimidine,

10 4-amino-5-(3-bromophenyl)-7-(6-(1,1-dioxidothiazolidin-3-yl)-3-pyridyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-thiomorpholinyl-3-pyridazinyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-(2,5-dihydropyrrolyl)-3-pyridyl)pyrido[2,3-d]pyrimidine,

15 4-amino-5-(3-bromophenyl)-7-(6-(1,3-dioxa-8-azaspiro[4.5]decan-8-yl)-3-pyridyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-hydroxy-3-pyridazinyl)pyrido[2,3-d]pyrimidine,

amino-5-(2,3-dichlorophenyl)-7-(6-(1,4-dioxa-8-azaspiro[4.5]decan-8-yl)-3-pyridyl)pyrido[2,3-d]pyrimidine,

20 4-amino-5-isopropyl-7-(6-(1,4-dioxa-8-azaspiro[4.5]decan-8-yl)-3-pyridyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-piperidinyl-3-pyridyl)pyrido[2,3-d]pyrimidine,

4-amino-5-(3-bromophenyl)-7-(6-(3-(4-tetrahydropyranyloxyimino)pyrrolidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine, and

25 4-amino-5-(2-trifluorophenylphenyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine and pharmaceutically acceptable salts and amides thereof. In addition, the partially hydrogenated or fully hydrogenated versions wherein the 5,6 and/or the 7,8 double bonds are hydrogenated of the compounds identified above are also included

30 within the scope of the invention. The preferred substitution pattern on the R³ group when

it is selected from, for example, a substituted aryl group, is having at least one substituent at the meta position. The preferred substitution pattern on the R⁴ position when it is selected from, for example, a substituted heterocycle or aryl group, is having at least one substituent at the para position. The present invention is therefore directed to compounds 5 of formula I or II with the variables recited as above wherein, in the case of R¹ selected from substituted aryl or heterocycle groups and R⁴ selected from substituted aryl or heterocycle groups, the substituents on the R³ group are meta and the substituents on the R⁴ group are para. In addition, the present invention encompasses pro-drugs of the above 10 compounds which may be active in their own right or are metabolized or converted to the non pro-drug form as exemplified above. The invention is not limited to synthetic versions of the claimed compounds and includes the compounds-per-se or pro-drugs or metabolites thereof regardless of how or where they are manufactured or made.

Definitions of Terms

15 The term "alkenyl," as used herein, refers to a straight or branched chain hydrocarbon containing from 2 to 6 carbons and containing at least one carbon-carbon double bond formed by the removal of two hydrogens. Representative examples of alkenyl include, but are not limited to, ethenyl, 2-propenyl, 2-methyl-2-propenyl, 3-but enyl, 4-pentenyl, 5-hexenyl, and the like.

20 The term "alkenyloxy," as used herein, refers to an alkenyl group, as defined herein, appended to the parent molecular moiety through an oxy moiety, as defined herein. Representative examples of alkenyloxy include, but are not limited to, 2-propenyloxy, 2-methyl-2-propenyloxy, 3-butenyloxy, 4-pentenyloxy, and the like.

25 The term "alkenyloxyimino," as used herein, refers to an alkenyloxy group, as defined herein, appended to the parent molecular moiety through an imino moiety, as defined herein. Representative examples of alkenyloxyimino include, but are not limited to, 2-propenyloxyimino, 2-methyl-2-propenyloxyimino, 3-butenyloxyimino, 4-pentenyloxyimino, and the like.

30 The term "alkenyloxyiminoalkyl," as used herein, refers to an alkenyloxyimino group, as defined herein, appended to the parent molecular moiety through an alkyl group,

as defined herein. Representative examples of alkenyloxyiminoalkyl include, but are not limited to, propen-2-yloxyiminomethyl, 2-[2-methylpropen-2-yloxyimino]ethyl, 2-[buten-3-yloxyimino]ethyl, 3-[penten-4-yloxyimino]propyl, and the like.

The term "alkoxy," as used herein, refers to an alkyl group, as defined herein,
5 appended to the parent molecular moiety through an oxy moiety, as defined herein. Representative examples of alkoxy include, but are not limited to, methoxy, ethoxy, propoxy, 2-propoxy, butoxy, tert-butoxy, pentyloxy, hexyloxy and the like.

The term "alkoxyalkoxy," as used herein, refers to an alkoxy group, as defined herein, appended to the parent molecular moiety through another alkoxy group, as defined
10 herein. Representative examples of alkoxyalkoxy include, but are not limited to, tert-butoxymethoxy, 2-ethoxyethoxy, 2-methoxyethoxy, methoxymethoxy, and the like.

The term "alkoxyalkoxyalkyl," as used herein, refers to an alkoxyalkoxy group, as defined herein, appended to the parent molecular moiety through an alkyl group, as defined herein. Representative examples of alkoxyalkoxyalkyl include, but are not limited
15 to, 2-(tert-butoxymethoxy)ethyl, 4-(2-ethoxyethoxy)butyl, 4-(2-methoxyethoxy)butyl, 2-(methoxymethoxy)ethyl, and the like.

The term "alkoxyalkoxyimino," as used herein, refers to an alkoxyalkoxy group, as defined herein, appended to the parent molecular moiety through an imino group, as defined herein. Representative examples of alkoxyalkoxyimino include, but are not limited
20 to, tert-butoxymethoxyimino, 2-(ethoxyethoxyimino), (2-methoxyethoxyimino), methoxymethoxyimino, and the like.

The term "alkoxyalkyl," as used herein, refers to an alkoxy group, as defined herein, appended to the parent molecular moiety through an alkyl group, as defined herein. Representative examples of alkoxyalkyl include, but are not limited to, tert-butoxymethyl,
25 2-ethoxyethyl, 2-methoxyethyl, methoxymethyl, and the like.

The term "alkoxyalkynyl," as used herein, refers to an alkoxy group, as defined herein, appended to the parent molecular moiety through an alkynyl group, as defined herein. Representative examples of alkoxyalkynyl include, but are not limited to, 3-(methoxy)propyn-1-yl, 4-(ethoxy)butyn-1-yl, and the like.

The term "alkoxyalkylcarbonyl," as used herein, refers to an alkoxyalkyl group, as defined herein, appended to the parent molecular moiety through a carbonyl group, as defined herein. Representative examples of alkoxyalkylcarbonyl include, but are not limited to, 2-(ethoxy)ethylcarbonyl, 2-(methoxy)ethylcarbonyl, and the like.

5 The term "alkoxycarbonyl," as used herein, refers to an alkoxy group, as defined herein, appended to the parent molecular moiety through a carbonyl group, as defined herein. Representative examples of alkoxy carbonyl include, but are not limited to, tert-butoxycarbonyl, ethoxycarbonyl, methoxycarbonyl, and the like.

10 The term "alkoxycarbonylalkenyl," as used herein, refers to one or two alkoxy carbonyl groups, as defined herein, appended to the parent molecular moiety through an alkenyl group, as defined herein. Representative examples of alkoxy carbonylalkenyl include, but are not limited to, 3-(methoxycarbonyl)propen-1-yl, , 4-(ethoxycarbonyl)buten-2-yl, 4-bis(ethoxycarbonyl)buten-2-yl, and the like.

15 The term "alkoxycarbonylalkoxy" as used herein refers to an alkoxy carbonyl group, as defined herein, appended to the parent molecular moiety through an alkoxy group. Representative examples of alkoxy carbonylalkoxy include methoxycarbonylmethoxy, ethoxycarbonylmethoxy, 2-(methoxycarbonyl)ethoxy, and the like.

20 The term "alkoxycarbonylalkoxyimino," as used herein refers to an alkoxy carbonylalkoxy group, as defined herein, appended to the parent molecular moiety through an imino group. Representative examples of alkoxy carbonylalkoxyimino include ethoxycarbonylmethoxyimino, 2-(methoxycarbonyl)ethoxyimino, and the like.

25 The term "alkoxycarbonylalkoxyiminoalkyl," as used herein refers to an alkoxy carbonylalkoxyimino group, as defined herein, appended to the parent molecular moiety through an alkyl group. Representative examples of alkoxy carbonylalkoxyiminoalkyl include 2-(ethoxycarbonylmethoxyimino)ethyl, 2-[2-(methoxycarbonyl)ethoxyimino]ethyl, and the like.

The term "alkoxycarbonylalkyl," as used herein, refers to an alkoxy carbonyl group, as defined herein, appended to the parent molecular moiety through an alkyl group, as

defined herein. Representative examples of alkoxycarbonylalkyl include, but are not limited to, 3-(methoxycarbonyl)propyl, , 4-(ethoxycarbonyl)butyl, and the like.

The term "alkoxyimino," as used herein, refers to an alkoxy group, as defined herein, appended to the parent molecular moiety through an imino group, as defined 5 herein. Representative examples of alkoxyimino include, but are not limited to, ethoxyimino, methoxyimino, propoxyimino, isopropoxyimino, and the like.

The term "alkoxyiminoalkyl," as used herein, refers to an alkoxyimino group, as defined herein, appended to the parent molecular moiety through an alkyl group, as defined herein. Representative examples of alkoxyiminoalkyl include, but are not limited 10 to, 2-(ethoxyimino)ethyl, 2-(methoxyimino)ethyl, 2-(propoxyimino)ethyl, 2-(isopropoxyimino)ethyl, and the like.

The term "alkyl," as used herein, refers to a straight or branched chain hydrocarbon containing from 1 to 6 carbon atoms. Representative examples of alkyl include, but are not limited to, methyl, ethyl, n-propyl, iso-propyl, n-butyl, sec-butyl, iso-butyl, tert-butyl, 15 n-pentyl, isopentyl, neopentyl, n-hexyl, and the like.

The term "alkylene," denotes a divalent group derived from a straight or branched chain hydrocarbon of from 1 to 3 carbon atoms. Representative examples of alkylene include, -CH₂-, -CH₂CH₂-, and -CH₂CH₂CH₂-.

The term "alkylcarbonyl," as used herein, refers to an alkyl group, as defined 20 herein, appended to the parent molecular moiety through a carbonyl group, as defined herein. Representative examples of alkylcarbonyl include, but are not limited, methylcarbonyl (acetyl), ethylcarbonyl, and the like.

The term "alkylcarbonyloxy," as used herein, refers to an alkylcarbonyl group, as defined herein, appended to the parent molecular moiety through an oxy group, as defined 25 herein. Representative examples of alkylcarbonyloxy include, but are not limited, methylcarbonyloxy, ethylcarbonyloxy, and the like.

The term "alkylcarbonyloxyalkoxy," as used herein, refers to an alkylcarbonyloxy group, as defined herein, appended to the parent molecular moiety through an alkoxy group, as defined herein. Representative examples of alkylcarbonyloxyalkoxy include, but 30 are not limited, 2-(methylcarbonyloxy)ethoxy, 3-(ethylcarbonyloxy)propoxy, and the like.

The term "alkylcarbonyloxyalkyl," as used herein, refers to an alkylcarbonyloxy group, as defined herein, appended to the parent molecular moiety through an alkyl group, as defined herein. Representative examples of alkylcarbonyloxyalkyl include, but are not limited, 2-(methylcarbonyloxy)ethyl, 3-(ethylcarbonyloxy)propyl, and the like.

5 The term "alkylcarbonyloxyalkylthio," as used herein, refers to an alkylcarbonyloxyalkyl group, as defined herein, appended to the parent molecular moiety through a thio moiety, as defined herein. Representative examples of alkylcarbonyloxyalkylthio include, but are not limited, 2-(methylcarbonyloxy)ethylsulfanyl, 3-(ethylcarbonyloxy)propylsulfoanyl, and the like.

10 The term "alkylsulfonyl," as used herein, refers to an alkyl group, as defined herein, appended to the parent molecular moiety through a sulfonyl group, as defined herein. Representative examples of alkylsulfonyl include, but are not limited, methylsulfonyl, ethylsulfonyl, and the like.

15 The term "alkylthio," as used herein, refers to an alkyl group, as defined herein, appended to the parent molecular moiety through a thio moiety, as defined herein. Representative examples of alkylthio include, but are not limited, methylsulfanyl, ethylsulfanyl, tert-butylsulfanyl, hexylsulfanyl, and the like.

20 The term "alkylthioalkyl," as used herein, refers to an alkylthio group, as defined herein, appended to the parent molecular moiety through an alkyl group, as defined herein. Representative examples of alkylthioalkyl include, but are not limited, methylsulfanyl methyl, 2-(ethylsulfanyl)ethyl, and the like.

25 The term "alkynyl," as used herein, refers to a straight or branched chain hydrocarbon group containing from 2 to 6 carbon atoms and containing at least one carbon-carbon triple bond. Representative examples of alkynyl include, but are not limited, to acetylenyl, 1-propynyl, 2-propynyl, 3-butynyl, 2-pentynyl, 1-butynyl and the like.

30 The term "amino," refers to an -NZ₁Z₂ group wherein Z₁ and Z₂ are appended to the parent molecular moiety through a nitrogen atom. Z₁ and Z₂ are independently selected from hydrogen, alkyl, alkylcarbonyl, benzyl, cycloalkyl, cycloalkylalkyl, formyl, and phenyl. Representative examples of -NZ₁Z₂ include, but are not limited to, amino,

benzylamino, methylamino, acetylamino, acetylmethyleamino, cyclopropylamino, cyclopropylmethyleamino, dimethylamino, phenylamino, and the like.

The term "aminoalkyl," as used herein, refers to an amino group, as defined herein, appended to the parent molecular moiety through an alkyl moiety, as defined herein.

5 Representative examples of aminoalkyl include, but are not limited, 3-aminopropyl, 4-dimethylaminobutyl, and the like.

The term "aminoalkylcarbonyl," as used herein, refers to an aminoalkyl group, as defined herein, appended to the parent molecular moiety through a carbonyl moiety, as defined herein. Representative examples of aminoalkylcarbonyl include, but are not limited, 3-(amino)propylcarbonyl, 4-(dimethylamino)butylcarbonyl, and the like.

10 The term "aminoalkynyl," as used herein, refers to an amino group, as defined herein, appended to the parent molecular moiety through an alkynyl moiety, as defined herein. Representative examples of aminoalkynyl include, but are not limited, 3-(amino)propyn-1-yl, 4-(dimethylamino)butyn-1-yl, and the like.

15 The term "amino-protecting group" or "N-protecting group," refers to groups intended to protect an amino group against undesirable reactions during synthetic procedures. Commonly used nitrogen-protecting groups are disclosed in Greene, T. W., & Wuts, P. G. M. (1991). *Protective Groups In Organic Synthesis* (2nd ed.). New York: John Wiley & Sons. Preferred nitrogen-protecting groups are formyl, acetyl, benzoyl, 20 pivaloyl, t-butyloxycarbonyl (Boc), and benzoyloxycarbonyl (Cbz).

25 The term "aminosulfonyl," as used herein, refers to an amino group, as defined herein, appended to the parent molecular moiety through a sulfonyl moiety, as defined herein. Representative examples of aminosulfonyl include, but are not limited, aminosulfonyl, dimethylaminosulfonyl, diethylaminosulfonyl, and the like.

The term "aryl," as used herein, refers to a monocyclic-ring system, or a bicyclic-fused ring system wherein one or both of the fused rings are aromatic. Representative examples of aryl include, but are not limited to, azulenyl, indanyl, indenyl, naphthyl, phenyl, tetrahydronaphthyl, and the like.

The aryl groups of this invention can be substituted with 1, 2, or 3 substituents independently selected from alkenyl, alkenyloxy, alkényloxyimino, alkényloxyiminoalkyl, alkoxy, alkoxyalkoxy, alkoxyalkoxyalkyl, alkoxyalkoxyimino, alkoxyalkyl, alkoxyalkynyl, alkoxy carbonyl, alkoxy carbonylalkenyl, alkoxy carbonylalkyl, 5 alkoxy carbonylalkoxyimino, alkoxy carbonylalkoxyiminoalkyl, alkoxyimino, alkoxyiminoalkyl, alkyl, alkylcarbonyl, alkylcarbonyloxy, alkylcarbonyloxyalkoxy, alkylcarbonyloxyalkyl, alkylcarbonyloxyalkylthio, alkylsulfonyl, alkylthio, alkylthioalkyl, aminoalkynyl, aminosulfonyl, azido, carboxy, carboxyalkyl, cyano, cyanoalkyl, cycloalkyl, cycloalkylalkoxy, cycloalkylalkyl, cycloalkyloxy, cycloalkyloxyimino, 10 ethylenedioxy, formyl, formylalkyl, haloalkyl, haloalkylcarbonyl, halogen, hydroxy, hydroxyalkoxy, hydroxyalkoxyalkyl, hydroxylalkyl, hydroxyimino, hydroxyiminoalkyl, methylenedioxy, methylenyl, nitro, oxo, 1-phenyl-1,3,8-triazaspiro[4.5]decan-4-one, 1-phenyl-1,3,8-triazaspiro[4.5]dec-2-en-4-one, phosphonato, spirocycle, (spirocycle)spirocycle, thioureylene, ureylene, -NZ₁₂Z₁₃, (NZ₁₂Z₁₃)alkyl, 15 (NZ₁₂Z₁₃)carbonyl, and (NZ₁₂Z₁₃)carbonyloxy wherein Z₁₂ and Z₁₃ are independently selected from hydrogen, alkoxyalkyl, alkyl, alkylcarbonyl, alkylsulfonyl, aminoalkylcarbonyl, aminosulfonyl, aryl, arylalkyl, arylalkylcarbonyl, cyanoalkyl, cycloalkyl, cycloalkylalkyl, formyl, haloalkylcarbonyl, heterocycle, heterocycloalkyl, heterocycloalkylcarbonyl, heterocyclesulfonyl, and (NZ₁₄Z₁₅)alkyl wherein Z₁₄ and Z₁₅ are 20 independently selected from the group consisting of hydrogen, alkoxyalkoxyalkyl, alkoxyalkyl, alkoxyalkylcarbonyl, alkyl, alkylcarbonyl, formyl, heterocycle, and hydroxyalkoxyalkyl.

The term "arylalkoxy," as used herein, refers to an aryl group, as defined herein, appended to the parent molecular moiety through an alkoxy group, as defined herein.

25 Representative examples of arylalkoxy include, but are not limited to, 2-phenylethoxy, 3-naphth-2-ylpropoxy, 5-phenylpentyloxy, and the like.

The term "arylalkoxycarbonyl," as used herein, refers to an arylalkoxy group, as defined herein, appended to the parent molecular moiety through a carbonyl group, as defined herein. Representative examples of arylalkoxycarbonyl include, but are not

30 limited to, benzoxycarbonyl, naphth-2-ylmethoxycarbonyl, and the like.

The term "arylalkoxyimino," as used herein, refers to an arylalkoxy group, as defined herein, appended to the parent molecular moiety through an imino group, as defined herein. Representative examples of arylalkoxyimino include, but are not limited to, 2-phenylethoxyimino, 3-naphth-2-ylpropoxymino, 5-phenylpentyloxyimino, and the like.

5 The term "arylalkyl," as used herein, refers to an aryl group, as defined herein, appended to the parent molecular moiety through an alkyl group, as defined herein. Representative examples of arylalkyl include, but are not limited to, benzyl, 2-phenylethyl, 3-phenylpropyl, 2-naphth-2-ylethyl, and the like.

10 The term "(aryl)alkyl," as used herein, refers to an aryl group, as defined herein, appended to the parent molecular moiety through another aryl group, as defined herein. Representative examples of (aryl)aryl include, but are not limited to, biphenyl, 4'-methoxybiphenyl, and the like.

15 The term "aryloxy," refers to an aryl group, as defined herein, appended to the parent molecular moiety through an oxy moiety, as defined herein. Representative examples of aryloxy include, but are not limited to, phenoxy, naphthoxy, 4-chlorophenoxy, 4-methylphenoxy, 3,5-dimethoxyphenoxy, and the like.

The term "azido," as used herein, refers to a -N₃ group.

The term "carbonyl," as used herein, refers to a -C(O)- group.

20 The term "carboxy," as used herein, refers to a -CO₂H group.

The term "carboxyalkyl," as used herein, refers to a carboxy group, as defined herein, appended to the parent molecular moiety through an alkyl group, as defined herein. Representative examples of carboxyalkyl include, but are not limited to, carboxymethyl, 2-carboxyethyl, 3-carboxypropyl, and the like.

25 The term "cyano," as used herein, refers to a -CN group.

The term "cyanoalkyl," as used herein, refers to a cyano group, as defined herein, appended to the parent molecular moiety through an alkyl group, as defined herein. Representative examples of cyanoalkyl include, but are not limited to, cyanomethyl, 2-cyanoethyl, 3-cyanopropyl, and the like.

The term "cycloalkyl," as used herein, refers to a saturated cyclic hydrocarbon group containing from 3 to 8 carbons. Representative examples of cycloalkyl include cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, cyclooctyl and the like.

The cycloalkyl groups of this invention can be substituted with 1 or 2 substituents

- 5 independently selected from alkenyl, alkenyloxy, alkenyloxyimino, alkenyloxyiminoalkyl, alkoxy, alkoxyalkoxy, alkoxyalkoxyalkyl, alkoxyalkoxyimino, alkoxyalkyl, alkoxyalkynyl, alkoxy carbonyl, alkoxy carbonylalkenyl, alkoxy carbonylalkyl, alkoxy carbonylalkoxyimino, alkoxy carbonylalkoxyiminoalkyl, alkoxyimino, alkoxyiminoalkyl, alkyl, alkyl carbonyl, alkyl carbonyloxy, alkyl carbonyloxyalkoxy,
- 10 alkyl carbonyloxyalkyl, alkyl carbonyloxyalkylthio, alkylsulfonyl, alkylthio, alkylthioalkyl, aminoalkynyl, aminosulfonyl, azido, carboxy, carboxyalkyl, cyano, cyanoalkyl, cycloalkyl, cycloalkylalkoxy, cycloalkylalkyl, cycloalkyloxy, cycloalkyloxyimino, ethylenedioxy, formyl, formylalkyl, haloalkyl, haloalkyl carbonyl, halogen, hydroxy, hydroxyalkoxy, hydroxyalkoxyalkyl, hydroxyalkyl, hydroxyimino, hydroxyiminoalkyl,
- 15 methylenedioxy, methylenyl, nitro, oxo, 1-phenyl-1,3,8-triazaspiro[4.5]decan-4-one, 1-phenyl-1,3,8-triazaspiro[4.5]dec-2-en-4-one, phosphonato, spirocycle, (spirocycle)spirocycle, thioureylene, ureylene, -(NZ₁₂Z₁₃), (NZ₁₂Z₁₃)alkyl, (NZ₁₂Z₁₃)carbonyl, and (NZ₁₂Z₁₃)carbonyloxy wherein Z₁₂ and Z₁₃ are independently selected from hydrogen, alkoxyalkyl, alkyl, alkyl carbonyl, alkylsulfonyl,
- 20 aminoalkyl carbonyl, aminosulfonyl, aryl, arylalkyl, arylalkyl carbonyl, cyanoalkyl, cycloalkyl, cycloalkylalkyl, formyl, haloalkyl carbonyl, heterocycle, heterocycle alkyl, heterocycle alkyl carbonyl, heterocyclesulfonyl, and (NZ₁₄Z₁₅)alkyl wherein Z₁₄ and Z₁₅ are independently selected from the group consisting of hydrogen, alkoxyalkoxyalkyl, alkoxyalkyl, alkoxyalkyl carbonyl, alkyl, alkyl carbonyl, formyl, heterocycle, and hydroxyalkoxyalkyl.
- 25

The term "cycloalkylalkoxy," as used herein, refers to cycloalkyl group, as defined herein, appended to the parent molecular moiety through an alkoxy group, as defined herein. Representative examples of cycloalkylalkoxy include, but are not limited to, cyclopropylmethoxy, 2-cyclobutylethoxy, cyclopentylmethoxy, cyclohexylmethoxy, 4-cycloheptylbutoxy, and the like.

The term "cycloalkylalkyl," as used herein, refers to cycloalkyl group, as defined herein, appended to the parent molecular moiety through an alkyl group, as defined herein. Representative examples of cycloalkylalkyl include, but are not limited to, 5 cyclopropylmethyl, 2-cyclobutylethyl, cyclopentylmethyl, cyclohexylmethyl and 4-cycloheptylbutyl, and the like.

The term "cycloalkylcarbonyl," as used herein, refers to cycloalkyl group, as defined herein, appended to the parent molecular moiety through a carbonyl group, as defined herein. Representative examples of cycloalkylcarbonyl include, but are not limited to, cyclopropylcarbonyl, 2-cyclobutylcarbonyl, cyclohexylcarbonyl, and the like.

10 The term "cycloalkyloxy," as used herein, refers to cycloalkyl group, as defined herein, appended to the parent molecular moiety through an oxy moiety, as defined herein. Representative examples of cycloalkyloxy include, but are not limited to, cyclopropyloxy, cyclopentyloxy, cyclohexyloxy, and the like.

The term "cycloalkyloxyimino," as used herein, refers to cycloalkyloxy group, as 15 defined herein, appended to the parent molecular moiety through an imino group, as defined herein. Representative examples of cycloalkyloxyimino include, but are not limited to, cyclopropyloxyimino, cyclopentyloxyimino, cyclohexyloxyimino, and the like.

The term "ethylenedioxy," as used herein, refers to a -OCH(R₂₀)CH(R₂₁)O- group 20 wherein the oxygen atoms of the ethylenedioxy group are attached to the parent molecular moiety through one carbon atom forming a 5 membered ring or the oxygen atoms of the ethylenedioxy group are attached to the parent molecular moiety through two adjacent carbon atoms forming a six membered ring. R₂₀ and R₂₁ are independently selected from hydrogen and alkyl or R₂₀ and R₂₁ together with the carbon atoms to which they are attached can join to form a 5 or 6 membered ring optionally containing 1 heteroatom 25 selected from NH, O, or S. Representative examples of ethylenedioxy include, but are not limited to, 3,5-dimethyl-1,2-cyclopentanediol, tetrahydro-3,4-furandiol, 1,2-cyclopentanediol, and the like.

The term "formyl," as used herein, refers to a -C(O)H group.

The term "formylalkyl," as used herein, refers to a formyl group, as defined herein, 30 appended to the parent molecular moiety through an alkyl group, as defined herein.

Representative examples of formylalkyl include, but are not limited to, formylmethyl, 2-formylethyl, and the like.

The term "halo" or "halogen," as used herein, refers to -Cl, -Br, -I or -F.

The term "haloalkoxy," as used herein, refers to at least one halogen, as defined herein, appended to the parent molecular moiety through an alkoxy group, as defined herein. Representative examples of haloalkoxy include, but are not limited to, chloromethoxy, 2-fluoroethoxy, trifluoromethoxy, pentafluoroethoxy, and the like.

The term "haloalkyl," as used herein, refers to at least one halogen, as defined herein, appended to the parent molecular moiety through an alkyl group, as defined herein.

10 Representative examples of haloalkyl include, but are not limited to, chloromethyl, 2-fluoroethyl, trifluoromethyl, pentafluoroethyl, 2-chloro-3-fluoropentyl, and the like.

The term "haloalkylcarbonyl," as used herein, refers to a haloalkyl group, as defined herein, appended to the parent molecular moiety through a carbonyl group, as defined herein. Representative examples of haloalkylcarbonyl include, but are not limited to, 2-fluoroethylcarbonyl, trifluoromethylcarbonyl, pentafluoroethylcarbonyl, and the like.

The term "heterocycle" as used herein, refers to a monocyclic, bicyclic, or tricyclic ring system. Monocyclic ring systems are exemplified by any 3- or 4-membered ring containing a heteroatom independently selected from oxygen, nitrogen and sulfur; or a 5-, 6- or 7-membered ring containing one, two or three heteroatoms wherein the heteroatoms 20 are independently selected from nitrogen, oxygen and sulfur. The 5-membered ring has from 0-2 double bonds and the 6- and 7-membered ring have from 0-3 double bonds. Representative examples of monocyclic ring systems include, but are not limited to, azetidinyl, azepinyl, aziridinyl, diazepinyl, 1,3-dioxolanyl, dioxanyl, dithianyl, furyl, imidazolyl, imidazolinyl, imidazolidinyl, isothiazolyl, isothiazolinyl, isothiazolidinyl, 25 isoxazolyl, isoxazolinyl, isoxazolidinyl, morpholinyl, oxadiazolyl, oxadiazolinyl, oxadiazolidinyl, oxazolyl, oxazolinyl, oxazolidinyl, piperazinyl, piperidinyl, pyranyl, pyrazinyl, pyrazolyl, pyrazolinyl, pyrazolidinyl, pyridyl, pyrimidinyl, pyridazinyl, pyrrolyl, pyrrolinyl, pyrrolidinyl, tetrahydrofuranyl, tetrahydrothiophenyl, tetrazinyl, tetrazolyl, thiadiazolyl, thiadiazolinyl, thiadiazolidinyl, thiazolyl, thiazolinyl, thiazolidinyl, 30 thiophenyl, thiomorpholinyl, 1,1-dioxidothiomorpholinyl, thiopyranyl, triazinyl, triazolyl,

trithianyl, and the like. Bicyclic ring systems are exemplified by any of the above monocyclic ring systems fused to an aryl group as defined herein, a cycloalkyl group as defined herein, or another monocyclic ring system. Bicyclic ring systems are further exemplified by any of the above monocyclic ring systems containing an alkylene of 1-3 carbon atoms attached to two non-adjacent carbon atoms of the monocyclic ring system. Representative examples of bicyclic ring systems include but are not limited to, for example, benzimidazolyl, benzothiazolyl, benzothiophenyl, benzoxazolyl, benzofuranyl, benzopyranyl, benzothiopyranyl, benzodioxinyl, 1,3-benzodioxolyl, cinnolinyl, hexahydro-1H-furo[3,4-c]pyrrolyl, indazolyl, indolyl, indolinyl, indolizinyl, naphthyridinyl, isobenzofuranyl, isobenzothiophenyl, isoindolyl, isoindolinyl, isoquinolyl, 2-oxa-5-azabicyclo[2.2.1]heptanyl, 1,4-dioxa-8-azaspiro[4.5]decanyl, 1,3-dioxa-8-azaspiro[4.5]decanyl, 1,5-dioxa-9-azaspiro[5.5]undecanyl, 1-oxa-4-thia-8-azaspiro[4.5]decanyl, 1-oxa-4,4-dioxa-4-thia-8-azaspiro[4.5]decanyl, 1-oxa-4-oxo-4-thia-8-azaspiro[4.5]decanyl, phthalazinyl, pyranopyridyl, 2,4-(1H,3H)-quinazolinedion-3-yl, quinolyl, quinolizinyl, quinoxalinyl, quinazolinyl, (3aR,6aS)-tetrahydro-3aH-[1,3]dioxolo[4,5-c]pyrrol-2-one, tetrahydroisoquinolyl, tetrahydroquinolyl, thiopyranopyridyl, and the like. Tricyclic rings systems are exemplified by any of the above bicyclic ring systems fused to an aryl group as defined herein, a cycloalkyl group as defined herein, or a monocyclic ring system. Representative examples of tricyclic ring systems include, but are not limited to, acridinyl, carbazolyl, carbolinyl, dibenzofuranyl, 2,4(1H,3H)-quinazolinedione, dibenzothiophenyl, 4,7-epoxy-7-methyl-2,3,3A,4,5,6,7,7a-octahydro-1H-isoindolyl, naphthofuranyl, naphthothiophenyl, oxanthrenyl, phenazinyl, phenoxathiinyl, phenoxazinyl, phenothiazinyl, thianthrenyl, thioxanthenyl, xanthenyl, and the like.

25 The heterocycles of this invention can be substituted with 1, 2, or 3 substituents independently selected from alkenyl, alkenyloxy, alkenyloxyimino, alkenyloxyiminoalkyl, alkoxy, alkoxyalkoxy, alkoxyalkoxyalkyl, alkoxyalkoxyimino, alkoxyalkyl, alkoxyalkynyl, alkoxycarbonyl, alkoxycarbonylalkenyl, alkoxycarbonylalkyl, alkoxycarbonylalkoxyimino, alkoxycarbonylalkoxyiminoalkyl, alkoxyimino, alkoxyiminoalkyl, alkyl, alkylcarbonyl, alkylcarbonyloxy, alkylcarbonyloxyalkoxy,

alkylcarbonyloxyalkyl, alkylcarbonyloxyalkylthio, alkylsulfonyl, alkylthio, alkylthioalkyl, aminoalkynyl, aminosulfonyl, azido, carboxy, carboxyalkyl, cyano, cyanoalkyl, cycloalkyl, cycloalkylalkoxy, cycloalkylalkyl, cycloalkyloxy, cycloalkyloxyimino, ethylenedioxy, formyl, formylalkyl, haloalkyl, haloalkylcarbonyl, halogen, hydroxy,

5 hydroxyalkoxy, hydroxyalkoxyalkyl, hydroxyalkyl, hydroxyimino, hydroxyiminoalkyl, methylenedioxy, methylenyl, nitro, oxo, phosphonato, spirocycle, (spirocycle)spirocycle, thioureylene, ureylene, -NZ₁₂Z₁₃, (NZ₁₂Z₁₃)alkyl, (NZ₁₂Z₁₃)carbonyl, and (NZ₁₂Z₁₃)carbonyloxy wherein Z₁₂ and Z₁₃ are independently selected from hydrogen, alkoxyalkyl, alkyl, alkylcarbonyl, alkylsulfonyl, aminoalkylcarbonyl, aminosulfonyl, aryl,

10 arylalkyl, arylalkylcarbonyl, cyanoalkyl, cycloalkyl, cycloalkylalkyl, formyl, haloalkylcarbonyl, heterocycle, heterocyclealkyl, heterocyclealkylcarbonyl, heterocyclesulfonyl, and (NZ₁₄Z₁₅)alkyl wherein Z₁₄ and Z₁₅ are independently selected from the group consisting of hydrogen, alkoxyalkoxyalkyl, alkoxyalkyl, alkoxyalkylcarbonyl, alkyl, alkylcarbonyl, formyl, heterocycle, and hydroxyalkoxyalkyl.

15 Representative examples include, but are not limited to 4,4-(*cis*-1,2-dioxycyclopentyl)piperidinyl,

The term "heterocyclealkoxy," as used herein, refers to a heterocycle group, as defined herein, appended to the parent molecular moiety through an alkoxy group, as defined herein. Representative examples of heterocyclealkoxy include, but are not limited

20 to, 2-pyrid-3-ylethoxy, 3-quinolin-3-ylpropoxy, 5-pyrid-4-ylpentyloxy, and the like.

The term "heterocyclealkoxyimino," as used herein, refers to a heterocyclealkoxy group, as defined herein, appended to the parent molecular moiety through an imino group, as defined herein. Representative examples of heterocyclealkoxyimino include, but are not limited to, 2-pyrid-3-ylethoxyimino, 3-quinolin-3-ylpropoxyimino, 5-pyrid-4-ylpentyloxyimino, 3-(4-morpholinyl)propoxyimino, and the like.

25 The term "heterocyclealkyl," as used herein, refers to a heterocycle, as defined herein, appended to the parent molecular moiety through an alkyl group, as defined herein. Representative examples of heterocyclealkyl include, but are not limited to, pyrid-3-ylmethyl, 2-pyrimidin-2-ylpropyl, and the like.

The term "heterocyclealkylcarbonyl," as used herein, refers to a heterocyclealkyl group, as defined herein, appended to the parent molecular moiety through a carbonyl group, as defined herein. Representative examples of heterocyclealkylcarbonyl include, but are not limited to, pyrid-3-ylmethylcarbonyl, 3-pyrimidin-2-ylpropylcarbonyl, and the like.

5 The term "(heterocycle)aryl," as used herein, refers to a heterocycle, as defined herein, appended to the parent molecular moiety through an aryl group, as defined herein. Representative examples of (heterocycle)aryl include, but are not limited to, 4-(pyridin-3-yl)phenyl, 4-(pyrimidin-2-yl)phenyl, and the like.

10 The term "heterocyclecarbonyl," as used herein, refers to a heterocycle, as defined herein, appended to the parent molecular moiety through a carbonyl group, as defined herein. Representative examples of heterocyclecarbonyl include, but are not limited to, pyrid-3-ylcarbonyl, quinolin-3-ylcarbonyl, and the like.

15 The term "heterocycleimino," as used herein, refers to a heterocycle group, as defined herein, appended to the parent molecular moiety through an imino group, as defined herein. Representative examples of heterocycleimino include, but are not limited to, 4-morpholinylimino, and the like.

20 The term "heterocycloxy," as used herein, refers to a heterocycle group, as defined herein, appended to the parent molecular moiety through an oxy moiety, as defined herein. Representative examples of heterocycloxy include, but are not limited to, pyrid-3-yloxy, quinolin-3-yloxy, and the like.

25 The term "heterocycloxyalkyl," as used herein, refers to a heterocycloxy group, as defined herein, appended to the parent molecular moiety through an alkyl group, as defined herein. Representative examples of heterocycloxyalkyl include, but are not limited to, pyrid-3-yloxymethyl, 2-quinolin-3-yloxyethyl, and the like.

The term "heterocycloxyimino," as used herein, refers to a heterocycloxy group, as defined herein, appended to the parent molecular moiety through an imino group, as defined herein. Representative examples of heterocycloxyimino include, but are not limited to, pyrid-3-yloxyimino, quinolin-3-yloxyimino, and the like.

The term "heterocycleoxyiminoalkyl," as used herein, refers to a heterocycleoxyimino group, as defined herein, appended to the parent molecular moiety through an alkyl group, as defined herein. Representative examples of heterocycleoxyiminoalkyl include, but are not limited to, 2-(pyrid-3-yloxyimino)ethyl, 2-5 (quinolin-3-yloxyimino)ethyl, and the like.

The term "heterocyclesulfonyl," as used herein, refers to a heterocycle, as defined herein, appended to the parent molecular moiety through a sulfonyl group, as defined herein. Representative examples of heterocyclesulfonyl include, but are not limited to, 10 pyrid-3-ylsulfonyl, quinolin-3-ylsulfonyl, 4-morpholinylsulfonyl, and the like.

The term "hydroxy," as used herein, refers to an -OH group.

The term "hydroxyalkoxy," as used herein, refers to one or two hydroxy groups, as defined herein, appended to the parent molecular moiety through an alkoxy group, as defined herein. Representative examples of hydroxyalkoxy include, but are not limited to, 15 2-hydroxyethoxy, 2,3-dihydroxypropoxy, 4-hydroxybutoxy, and the like.

The term "hydroxyalkoxyalkyl," as used herein, refers to a hydroxyalkoxy group, as defined herein, appended to the parent molecular moiety through an alkyl group, as defined herein. Representative examples of hydroxyalkoxyalkyl include, but are not limited to, 20 2-[2-(hydroxyethoxy]ethyl, 2-[3-(hydroxy)propoxy]ethyl, 4-hydroxybutoxymethyl, and the like.

The term "hydroxyalkyl," as used herein, refers to one or two hydroxy groups, as defined herein, appended to the parent molecular moiety through an alkyl group, as defined herein. Representative examples of hydroxyalkyl include, but are not limited to, 25 2-hydroxyethyl, 2,3-dihydroxypropyl, and the like.

The term "hydroxyimino," as used herein, refers to a HON= group.

The term "hydroxyiminoalkyl," as used herein, refers to a hydroxyimino group, as defined herein, appended to the parent molecular moiety through an alkyl group, as defined herein. Representative examples of hydroxyiminoalkyl include, but are not limited to, 30 2-(hydroxyimino)ethyl, 3-(hydroxyimino)propyl, and the like.

The term "imino," as used herein, refers to a HN= group.

The term "mammal," has its ordinary meaning and includes human beings.

The term "methylenedioxy," as used herein, refers to a -OCH₂O- group wherein the oxygen atoms of the methylenedioxy are attached to the parent molecular moiety through two adjacent carbon atoms forming a 5 membered ring. The carbon atom of methylenedioxy group is optionally substituted with one substituent selected from alkyl and oxo.

5 The term "methyleneyl," as used herein refers to a H₂C= group.

The term "nitro," as used herein, refers to a -NO₂ group.

The term "oxo," as used herein, refers to a O= moiety.

The term "oxy," as used herein, refers to a -O- moiety.

10 The term "phosphonato," refers to a (R₉O)₂P(O)O- group wherein R₉ is alkyl.

The term "spirocycle," as used herein, refers to a -X₁(CH₂)_pX₂- group wherein X₁ and X₂ are independently selected from CH₂, NH, O, S, S(O), and S(O)₂; and p is an integer from 2-3. X₁ and X₂ are attached to the parent molecular moiety through one carbon atom forming a 5 or 6 membered ring. Representative examples of spirocycle 15 include, but are not limited to 1,3-dioxolane, 1,3-dioxane, 1,3-oxathiane, 1,3-oxazinane, and the like.

The spirocycles of this invention are optionally substituted with 1, 2, or 3 substituents independently selected from alkoxy, alkoxyalkyl, alkoxy carbonyl, alkyl, alkyl carbonyl, aminocarbonyl, benzyloxycarbonyl, and formyl. The substituents can be 20 attached to nitrogen or any of the carbon atoms.

The term "(spirocycle)spirocycle," as used herein, refers to a spirocycle, as defined herein, attached to the parent molecular moiety through a spirocycle, as defined herein. Representative examples of spirocycle-spirocycle include, but are not limited to, 1,7,9-trioxa spiro[4.5]decane, 1,4,7,9-tetraoxa spiro[4.5]decane, and the like.

25 The term "thio," as used herein, refers to a -S- moiety.

The term "thioureylene," as used herein, refers to -NR₉₇C(S)NR₉₈R₉₉, wherein R₉₇, R₉₈, and R₉₉ are independently selected from hydrogen, alkyl, aryl, and arylalkyl, as defined herein.

The term "ureylene," as used herein, refers to $-\text{NR}_{97}\text{C}(\text{O})\text{NR}_{98}\text{R}_{99}$, wherein R_{97} , R_{98} , and R_{99} are independently selected from hydrogen, alkyl, aryl, and arylalkyl, as defined herein.

5 In a further aspect of the present invention pharmaceutical compositions are disclosed which comprise a compound of the present invention in combination with a pharmaceutically acceptable carrier.

The present invention includes one or more compounds, as set forth above, formulated into compositions together with one or more non-toxic physiologically tolerable or acceptable diluents, carriers, adjuvants or vehicles that are collectively 10 referred to herein as diluents, for parenteral injection, for oral administration in solid or liquid form, for rectal or topical administration, or the like. As is well known in the art, a compound of the present invention can exist in a variety of forms including pharmaceutically-acceptable salts, amides and the like.

15 Compositions may be prepared that will deliver the correct amount of a compound or compounds of the invention. The following dosages are thought to provide the optimal therapy: iv infusions: 0.1- 250 nmol/kg/minute, preferably from 1-50 nmol/kg/minute; oral: 0.01-250 $\mu\text{Mol}/\text{kg}/\text{day}$, preferably from about 0.1-50 $\mu\text{Mol}/\text{kg}/\text{day}$; these oral molar dosage ranges correspond to 0.005-125 mg/kg/day, preferably 0.05-25 mg/kg/day. For treatment of acute disorders the preferred route of administration is intravenous; the 20 preferred method of treating chronic disorders is orally by means of a tablet or sustained release formulation.

“Pharmaceutically-acceptable amide” refers to the pharmaceutically-acceptable, nontoxic amides of the compounds of the present invention which include amides formed with suitable organic acids or with amino acids, including short peptides consisting of 25 from 1-to-6 amino acids joined by amide linkages which may be branched or linear, wherein the amino acids are selected independently from naturally-occurring amino acids, such as for example, glycine, alanine, leucine, valine, phenylalanine, proline, methionine, tryptophan, asparagine, aspartic acid, glutamic acid, glutamine, serine, threonine, lysine, arginine, tyrosine, histidine, ornithine, and the like.

"Pharmaceutically acceptable salts" refers to the pharmaceutically-acceptable, nontoxic, inorganic or organic acid addition salts of the compounds of the present invention, as described in greater detail below.

Compounds of the present invention can exist as stereoisomers wherein 5 asymmetric or chiral centers are present. These compounds are designated by the symbols "R" or "S," depending on the configuration of substituents around the chiral carbon atom. The present invention contemplates various stereoisomers and mixtures thereof. Stereoisomers include enantiomers and diastereomers. Individual stereoisomers of compounds of the present invention can be prepared synthetically from commercially 10 available starting materials which contain asymmetric or chiral centers or by preparation of racemic mixtures followed by resolution well-known to those of ordinary skill in the art. These methods of resolution are exemplified by (1) attachment of a mixture of enantiomers to a chiral auxiliary, separation of the resulting mixture of diastereomers by recrystallization or chromatography and liberation of the optically pure product from the 15 auxiliary or (2) direct separation of the mixture of optical enantiomers on chiral chromatographic columns.

The compounds of the present invention can be used in the form of pharmaceutically-acceptable salts derived from inorganic or organic acids. These salts include, but are not limited to, the following: acetate, adipate, alginate, aspartate, 20 benzoate, benzenesulfonate, bisulfate, butyrate, camphorate, camphorsulfonate, citrate, cyclopentanepropionate, digluconate, dodecylsulfate, ethanesulfonate, flavianate, fumarate, glucoheptonate, glycerophosphate, hemisulfate, heptonate, hexonoate, hydrochloride, hydrobromide, hydroiodide, 2-hydroxy-ethanesulfonate, lactate, maleate, methanesulfonate, nicotinate, 2-naphthalenesulfonate, oxalate, palmoate, pectinate, 25 persulfate, 3-phenylpropionate, phosphate, picrate, pivalate, propionate, succinate, tartrate, thiocyanate, tosylate, and undecanoate.

Appropriate cationic salts are also readily prepared by conventional procedures such as treating an acid of Formula I with an appropriate amount of base, such as an alkali or alkaline earth metal hydroxide, e.g., sodium, potassium, lithium, calcium, or 30 magnesium, or an organic base such as an amine, e.g., dibenzylethylenediamine,

cyclohexylamine, dicyclohexylamine, triethylamine, piperidine, pyrrolidine, benzylamine, and the like, or a quaternary ammonium hydroxide such as tetramethylammonium hydroxide and the like. Also, the basic nitrogen-containing groups can be quaternized with such agents as loweralkyl halides, such as methyl, ethyl, propyl, and butyl chlorides, 5 bromides, and iodides; dialkyl sulfates; long chain halides such as decyl, lauryl, myristyl, and stearyl chlorides, bromides and iodides; arylalkyl halides like benzyl and phenethyl bromides, and others. Water or oil-soluble or dispersible products are thereby obtained.

The salts of the present invention can be synthesized from the compounds of Formula I which contain a basic or acidic moiety by conventional methods, such as by 10 reacting the free base or acid with stoichiometric amounts or with an excess of the desired salt forming inorganic acid or base in a suitable solvent or various combinations of solvents.

Further included within the scope of the present invention are pharmaceutical compositions comprising one or more of the compounds of formula I prepared and 15 formulated in combination with one or more non-toxic pharmaceutically acceptable carriers compositions, in the manner described below.

Compositions suitable for parenteral injection may comprise pharmaceutically acceptable sterile aqueous or nonaqueous solutions, dispersions, suspensions or emulsions and sterile powders for reconstitution into sterile injectable solutions or dispersions. 20 Examples of suitable aqueous and nonaqueous carriers, diluents, solvents or vehicles include water, ethanol, polyols (propylene glycol, polyethylene glycol, glycerol, and the like), suitable mixtures thereof, vegetable oils (such as olive oil) and injectable organic esters such as ethyl oleate. Proper fluidity may be maintained, for example, by the use of a coating such as lecithin, by the maintenance of the required particle size in the case of 25 dispersions, and by the use of surfactants.

These compositions may also contain adjuvants such as preserving, wetting, emulsifying, and dispersing agents. Prevention of the action of microorganisms may be ensured by various antibacterial and antifungal agents, for example, parabens, chlorobutanol, phenol, sorbic acid, and the like. It may also be desirable to include 30 isotonic agents, for example, sugars, sodium chloride and the like. Prolonged absorption

of the injectable pharmaceutical form may be brought about by the use of agents delaying absorption, for example, aluminum monostearate and gelatin.

If desired, and for more effective distribution, the compounds may be incorporated into slow-release or targeted-delivery systems, such as polymer matrices, liposomes, and 5 microspheres. They may be sterilized, for example, by filtration through a bacteria-retaining filter, or by incorporating sterilizing agents in the form of sterile solid compositions, which may be dissolved in sterile water, or some other sterile injectable medium immediately before use.

Solid dosage forms for oral administration may include capsules, tablets, pills, 10 powders, and granules. In such solid dosage forms, the active compound is admixed with at least one inert customary excipient (or carrier), such as sodium citrate or dicalcium phosphate, and additionally (a) fillers or extenders, as for example, starches, lactose, sucrose, glucose, mannitol and silicic acid; (b) binders, as for example, carboxymethylcellulose, alginates, gelatin, polyvinylpyrrolidone, sucrose and acacia; (c) 15 humectants, as for example, glycerol; (d) disintegrating agents, as for example, agar-agar, calcium carbonate, potato or tapioca starch, alginic acid, certain complex silicates and sodium carbonate; (e) solution retarders, as for example paraffin; (f) absorption accelerators, as for example, quaternary ammonium compounds; (g) wetting agents, as for example, cetyl alcohol and glycerol monostearate; (h) adsorbents, as for example, kaolin 20 and bentonite; and (i) lubricants, as for example, talc, calcium stearate, magnesium stearate, solid polyethylene glycols, sodium lauryl sulfate or mixtures thereof. In the case of capsules, tablets and pills, the dosage forms may also comprise buffering agents.

Solid compositions of a similar type may also be employed as fillers in soft and hard-filled gelatin capsules, using such excipients as lactose or milk sugar, as well as high 25 molecular weight polyethylene glycols, and the like.

Solid dosage forms such as tablets, dragees, capsules, pills and granules may be prepared with coatings and shells, such as enteric coatings and others well known in this art. They may contain pacifying agents, and may also be of such composition that they release the active compound or compounds in a certain part of the intestinal tract in a

delayed manner. Examples of embedding compositions which may be used are polymeric substances and waxes.

The active compounds may also be in micro-encapsulated form, if appropriate, with one or more of the above-mentioned excipients.

5 Liquid dosage forms for oral administration include pharmaceutically acceptable emulsions, solutions, suspensions, syrups and elixirs. In addition to the active compounds, the liquid dosage forms may contain inert diluents commonly used in the art, such as water or other solvents, solubilizing agents and emulsifiers, as for example, ethyl alcohol, isopropyl alcohol, ethyl carbonate, ethyl acetate, benzyl alcohol, benzyl benzoate, 10 propylene glycol, 1,3-butylene glycol, dimethylformamide, oils, in particular, cottonseed oil, groundnut oil, corn germ oil, olive oil, castor oil and sesame oil, glycerol, tetrahydrofurfuryl alcohol, polyethylene glycols and fatty acid esters of sorbitan or mixtures of these substances, and the like.

15 Besides such inert diluents, these liquid dosage forms may also include adjuvants, such as wetting agents, emulsifying and suspending agents, sweetening, flavoring and perfuming agents.

20 Suspensions, in addition to the active compounds, may contain suspending agents, as for example, ethoxylated isostearyl alcohols, polyoxyethylene sorbitol and sorbitan esters, microcrystalline cellulose, aluminum metahydroxide, bentonite, agar-agar and tragacanth, or mixtures of these substances, and the like.

25 Compositions for rectal or vaginal administrations are preferably suppositories which can be prepared by mixing the compounds of this invention with suitable non-irritating excipients or carriers such as cocoa butter, polyethylene glycol or a suppository wax, which are solid at ordinary temperatures but liquid at body temperature and therefore, melt in the rectum or vaginal cavity and release the active component.

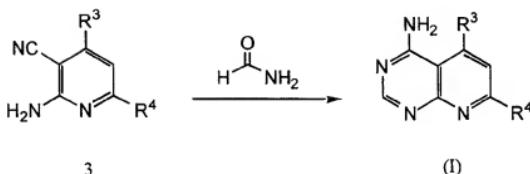
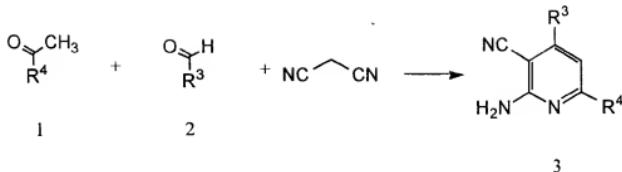
30 Dosage forms for topical or transdermal administration of a compound of this invention further include ointments, pastes, creams, lotions, gels, powders, solutions, sprays, inhalants or transdermal patches. Transdermal administration via a transdermal patch is a particularly effective and preferred dosage form of the present invention. The active component is admixed under sterile conditions with a pharmaceutically acceptable

carrier and any needed preservative, buffers or propellants as may be required. It is known that some agents may require special handling in the preparation of transdermal patch formulations. For example, compounds that are volatile in nature may require admixture with special formulating agents or with special packaging materials to assure proper 5 dosage delivery. In addition, compounds which are very rapidly absorbed through the skin may require formulation with absorption-retarding agents or barriers. Ophthalmic formulations, eye ointments, powders and solutions are also contemplated as being within the scope of this invention.

The present compounds may also be administered in the form of liposomes. As is 10 known in the art, liposomes are generally derived from phospholipids or other lipid substances. Liposomes are formed by mono- or multi-lamellar hydrated liquid crystals that are dispersed in an aqueous medium. Any non-toxic, physiologically acceptable and metabolizable lipid capable of forming liposomes may be used. The present compositions in liposome form may contain, in addition to the compounds of the present invention, 15 stabilizers, preservatives, excipients, and the like. The preferred lipids are the phospholipids and the phosphatidyl cholines (lecithins), both natural and synthetic. Methods to form liposomes are known in the art. See, for example, Prescott, Ed., Methods in Cell Biology, Volume XIV, Academic Press, New York, N. Y., (1976), p 33 et seq.

20 Synthetic Methods

The compounds and processes of the present invention will be better understood in connection with the following synthetic schemes which illustrate the methods by which the compounds of the invention may be prepared. The R groups are as defined above unless otherwise noted below.

Scheme 1

The compounds of the present invention may be synthesized by methods illustrated in Schemes 1 and 2. In accordance with Scheme 1, the 5,7-disubstituted compounds wherein R⁴ and R³ are aryl or a heterocyclic group may be prepared by a modification of a method of Kambe et al., *Synthesis*, 1980, 366-368. An appropriately substituted acetophenone (1, the "R⁴ Reagent"), wherein R⁴ is aryl or a heterocyclic group, an appropriately substituted aldehyde (2, the "R³ Reagent"), R³ is aryl or a heterocyclic group, and malononitrile are heated in the presence of ammonium acetate, or another suitable ammonium salt, such as for example, ammonium propionate, ammonium iodide, or the like, in an aprotic solvent to produce compound (3). The water of the reaction may be removed by use of a Dean Stark apparatus or by another suitable means, such as 4 Å molecular sieves. Suitable aprotic solvents include benzene, toluene, methylene chloride, DMF, THF, dioxane, and the like. The reaction may be performed at from about 40 °C to about 200 °C, and preferably at the reflux temperature of the solvent, for from about 1 hour to about 24 hours, preferably about 4 hours to 8 hours. The product (3) is preferably purified by chromatography after isolation from the reaction mixture. The above reaction may also proceed by contacting the aldehyde (2) with malononitrile and isolating the

resulting dicyano R^3 substituted alkene which is then reacted with the ketone (1) to form, upon addition of ammonium and cyclization, compound (3). Aliphatic aldehydes do not work effectively by this route. The ketone (1) may, however, include R^4 as alkyl groups.

The acetophenone starting materials (1) may be obtained commercially, or

5 prepared easily by Friedel-Craft acylation of a suitable aromatic substrate, for example. The appropriate aldehyde starting materials (2) also may be obtained commercially, or may be prepared easily, for example by reductions of esters or acids with DIBAL or another suitable hydride reducing agent, or oxidation of alcohols under Swern conditions, for example.

10 Compound (3) is then treated with excess formamide by heating at reflux. The formation of product is monitored by TLC, and when the reaction is complete (after about 1 to about 8 hours) the reaction mixture is cooled to room temperature. The 5,7-disubstituted pyrido[2,3-d]pyrimidine product I is then removed by filtration and purified by column chromatography. This compound may then be partially or fully reduced by

15 catalytic hydrogenation to the partially saturated or fully saturated version(s) (on the right side of the molecule) of the compounds shown in Scheme 1 or of Formula I. Stereoisomers produced during these reduction steps are included within the scope of the invention. The present invention also contemplates reductions which produce single bonds between the 5,6 and 7,8 positions and a double bond between the 6,7 carbons. The

20 stereoisomers may be isolated and purified by conventional means.

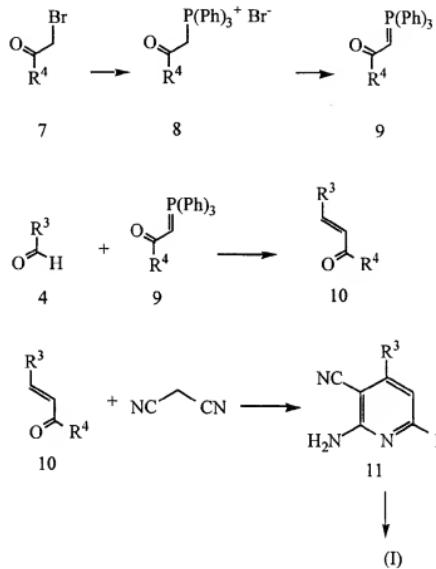
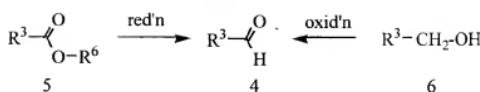
In accordance with Scheme 2 are prepared compounds of Formula I wherein R^4 is preferably an aryl, heterocycle or heterocyclic group, and R^3 is loweralkyl, loweralkenyl, loweralkynyl, or an arylalkyl group. In addition, R^4 may be selected from those additional groups listed in R^3 .

25 Compound (4, the " R^3 Reagent") may be obtained commercially or prepared from the precursor ester (5) or alcohol (5) by suitable reactions. Compound (5) may be reduced with a suitable reducing agent, such as for example, diisobutylaluminum hydride or another similar alkylaluminum hydride, under conditions well known to the art. Compound (6) may be oxidized to the aldehyde (4) Swern oxidation conditions, or other

reactions known to those skilled in the art. The desired compound (4) is freshly prepared before its use in the reaction described below.

Compound (9), the "R⁴ Reagent" may be prepared from the precursor alpha-bromo ketone (7) by a two-step procedure. Compound (7) is treated with triphenylphosphine in 5 the presence of a base, such as for example, triethyl amine, to give compound (8). Compound (8) is then treated with an alkali metal base, such as NaOH or the like, to give compound (9). The procedure is normally accomplished by vigorous mixing of a solution of (8) in an organic solvent with an aqueous solution of base.

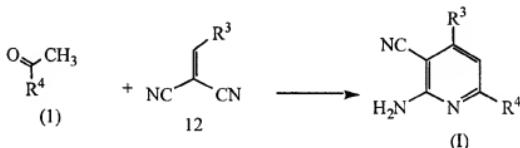
Compounds (4) and (9) are mixed and the mixture is held at ambient temperature 10 until the reaction is complete (monitoring by TLC), and the product (10) is purified by chromatography. A mixture of the cis and trans isomers is obtained and taken to the next step without further separation. Compound (10) is condensed with malononitrile by heating in the presence of ammonium acetate as defined for Scheme 1 above to produce compound (11).

Scheme 2

Compound (11) is then treated with excess formamide by heating at reflux. The formation of product is monitored by TLC, and when the reaction is complete (routinely, after about 1 to about 8 hours) the reaction mixture is cooled to room temperature. The 5,7-disubstituted pyrido[2,3-d]pyrimidine product I is then removed by filtration and purified by column chromatography. In an alternate procedure, compound (11) is treated by heating with formamidine acetate in ethoxyethanol, followed by purification by flash chromatography. In another alternate procedure, compound (11) and ammonium sulfate

are heated at reflux in triethyl orthoformate for about 1 to about 8 hours, but preferably about 2 hours. The reaction mixture is cooled and added to a mixture of ammonia in ethanol. The mixture is stirred for about 12 to 24 hours at 25 °C, then at reflux for from one to 4 hours, and the solvent is removed in vacuo. The residue is purified by trituration with chloroform/ethyl acetate, and the product may be converted to a hydrochloride salt by suspension in 3M HCl, followed by lyophilization.

10

Scheme 3

Scheme 3 illustrates an alternate method for preparing the compounds I of the invention. Compounds (1), prepared as described above, are reacted with a dicyanoalkene compound (12) by heating with a suitable ammonium salt, such as for example, ammonium acetate, ammonium propionate, ammonium iodide, or the like, at reflux in an 15 alcoholic or aprotic solvent to give the compound I. Suitable solvents for the reaction may be easily determined by those skilled in the art, without undue trial and error, and may include, for example, ethanol, propanol, isopropanol, t-butanol, n-butanol, 1,2-dichloroethane, benzene, chloroform, carbon tetrachloride, toluene, dioxane, dimethoxyethane, and the like. A preferred solvent is 1,2-dichloroethane. The dicyano 20 compounds (12) may be prepared from the precursor aldehyde (4) by treatment with malononitrile in 1:1 H₂O:EtOH in the presence of a catalytic amount of glycine according to the method of Bastus (Tetrahedron Lett., 1963: 955), or alternately MgO in dichloromethane or a similar aprotic solvent (cf. Broekhuis, et al., Recl. J. R. Neth. Chem. Soc., 99: 6-12 (1980); Moison, et al. Tetrahedron (1987), 43:537-542).

To prepare compounds of formula I wherein R¹ and R² are not both hydrogen atoms, it is possible to prepare the desired derivative from the compound of Formula I wherein R¹ and R² are both hydrogen atoms. When R¹ or R² is loweralkyl this may be

accomplished by reaction of the free amino group with the appropriate alkylating reagent, such as an alkyl halide, an alkyl mesylate or an alkyl tosylate, for example, in the presence of a base such as triethylamine or potassium carbonate in a suitable solvent, such as for example, methylene chloride or THF. When R¹ or R² is arylalkyl this may be

5 accomplished by reaction of the free amino group with the appropriate arylalkyl halide, an alkyl mesylate or an alkyl tosylate, for example, in the presence of a base such as triethylamine or potassium carbonate in a suitable solvent, such as for example, methylene chloride or THF. When R¹ or R² is acyl this may be accomplished by reaction of the free amino group with the appropriate acid anhydride, acyl chloride or activated acyl group, in

10 the presence of a base such as triethylamine or potassium carbonate in a suitable solvent, such as for example, methylene chloride or THF. When R¹ and R² are taken together with the nitrogen atom to which they are attached to form a 5-to-7 membered ring optionally containing an additional oxygen or nitrogen atom, the compound may be prepared by reacting a precursor compound having a halogen atom in place of the amino group at the

15 4-position with a 5-7 membered ring compound optionally containing an additional oxygen or nitrogen atom. Examples of such compounds include, but are not limited to, morpholine, piperidine, pyrrolidine, piperazine, thiomorpholine, and the like. Also, this alternate procedure may be used to prepare alkyl substituted amino compounds, for example by reacting the chloro compound with a mono- or disubstituted amine, such as

20 for example, diethylamine, allyl amine, dibutylamine. This reaction takes place readily in a solvent such as methylene chloride, for example, in the presence of a tertiary amine. The precursor compound having a halogen atom in place of the amino group at the 4-position may be prepared by substitution of triethyl orthoformate for the formamide followed by chlorination of the ring by treatment with phosphorous oxychloride or thionyl chloride in

25 the presence of DMF in Scheme 1 wherein compound (3) is converted to compound I.

Method of Inhibiting Kinase

In yet another aspect of the present invention a process of inhibiting adenosine kinase is disclosed. In accordance with that process, an adenosine kinase enzyme is exposed to an effective inhibiting amount of an adenosine kinase inhibitor compound of

the present invention. Means for determining an effective inhibiting amount are well known in the art.

The adenosine kinase to be inhibited can be located in vitro, in situ or in vivo. Where the adenosine kinase is located in vitro, adenosine kinase is contacted with the 5 inhibitor compound, typically by adding the compound to an aqueous solution containing the enzyme, radiolabeled substrate adenosine, magnesium chloride and ATP. AK activity of cell supernatants was assayed radiometrically. Assays were carried out at ambient temperature in a final volume of 100 μ L. The reaction mixture contained 64 mM Tris HCl (pH 7.5), 0.2 mM MgCl₂, 1 mM ATP, 0.2 μ M U-[¹⁴C]-adenosine or [³H]-adenosine and 10 appropriate volumes of rat brain cytosol as a source of adenosine kinase. The reaction was terminated after 15 min by spotting 40 μ L of the reaction mixture onto disks of Whatman DE-81 anion exchange paper. DE-81 disks were then air-dried, washed for 10 minutes in 2 mM ammonium formate, then rinsed successively with distilled water, methanol and acetone, and dried. DE-81 disks were then soaked for 5 minutes in 0.1N HCl/0.4 M KCl 15 before addition of scintillation cocktail and counting by liquid scintillation counting. The enzyme can exist in intact cells or in isolated subcellular fractions containing the enzyme. The enzyme is then maintained in the presence of the inhibitor for a period of time and under suitable physiological conditions. Means for determining maintenance times are well known in the art and depend inter alia on the concentrations of enzyme and the 20 physiological conditions. Suitable physiological conditions are those necessary to maintain adenosine kinase viability and include temperature, acidity, tonicity and the like. Inhibition of adenosine kinase can be performed, by example, according to standard procedures well known in the art (Yamada, et al., *Comp. Biochem. Physiol.*, (1982), 71B, 367-372), hereby incorporated by reference.

25 In vitro adenosine kinase activity can be measured using any of the standard procedures well known in the art. By way of example, cells containing adenosine kinase, such as IMR-32 human neuroblastoma cells, are incubated in the presence and absence of an inhibitor. Inhibition is measured as the ability to inhibit phosphorylation of externally applied ¹⁴C-adenosine by these cells. The cells can be intact or broken. The specificity of 30 adenosine kinase inhibitory activity is determined by studying the effects of inhibitors on

adenosine A₁, A_{2A}, and A₃ receptor binding, adenosine deaminase activity and adenosine transport.

Where the adenosine kinase is located *in situ* or *in vivo*, the inhibiting compound is typically administered to a fluid perfusing the tissue containing the enzyme. That fluid 5 can be a naturally occurring fluid such as blood or plasma or an artificial fluid such as saline, Ringer's solution and the like.

Numerous animal models for studying adenosine kinase activity and the effects of inhibiting such activity are well known in the art. By way of example, adenosine kinase inhibitors have been reported to protect rodents (e.g., mice and rats) from experimentally-induced seizure activity (Zhang, G., Murray, T.F., J. Pharmacol. Exp. Ther., 1993, 264, 10 1415-1424; Murray, T.F., et al., Drug Dev. Res., 1993, 28, 410-415; Kowaluk, E. A., et al., Drug Dev. Res., 1996, 37, 190), hereby incorporated by reference. Other animal models of adenosine kinase activity have been described (See, e.g., Davies, et al., Biochem. Pharmacol., 1984, 33, 347-355; Keil, et al., Eur. J. Pharmacol., 1994, 271, 37-15 46; Murray, et al., Drug Development Res., 1993, 28, 410-415), hereby incorporated by reference.

A method of inhibiting adenosine kinase *in vivo* is particularly useful in mammals such as humans. Administering a therapeutic amount of an inhibitor compound is typically accomplished by the parenteral (e.g., intravenous injection) or oral administration 20 of the compound.

By a "therapeutically-effective amount" of the compound of the invention is meant a sufficient amount of the compound to treat adenosine kinase related disorders or those conditions or diseases which are ameliorated or modified by local inhibition of the enzyme which results in an increase in the concentration of adenosine. It will be understood, 25 however, that the total daily usage of the compounds and compositions of the present invention is to be decided by the attending physician within the scope of sound medical judgment. The specific therapeutically-effective dose level for any particular patient will depend upon a variety of factors including the disorder being treated and the severity of the disorder; activity of the specific compound employed; the specific composition 30 employed; the age, body weight, general health, gender and diet of the patient; the time of

administration, route of administration, and rate of excretion of the specific compound employed; the duration of the treatment; drugs used in combination or coincidental with specific compound employed; and the like factors well known in the medical arts and well within the capabilities of attending physicians.

5 The compounds of the invention were tested in vivo in the hot plate test of analgesia in mammals such as mice. For example, the compounds of examples 6, 79, 104, 130, 133, 134, 137, 205, 246 and 256 in the procedure described directly below were tested thirty minutes after pretreatment with the drugs (30 μ mol/kg i.p.) for latency to 10th jump (in seconds). The longer the number of seconds, the more effective the drug at
10 masking the pain felt from the hot plate. Compound 6 resulted in 152 seconds relative to the vehicle alone of 72.8 ± 10.5 seconds (average \pm standard deviation); compound 79 resulted in 143 seconds; compound 104 resulted in 180 seconds; compound 130 resulted in 158 seconds; compound 133 resulted in 131 seconds; compound 134 resulted in 137 seconds; compound 137 resulted in 159 seconds; compound 205 resulted in 158 seconds,
15 compound 246 resulted in 160 seconds and compound 256 resulted in 143 seconds.
Compounds of the invention are therefore potent pain relievers as demonstrated in this animal model.

Mouse Hot Plate Assay

20 Male CF1 mice (Charles River) of approximately 25-30 g body weight are pretreated with 10 ml/kg of the test compounds, i.p. or p.o., in groups of 8 animals per dose. At the end of the pretreatment period, the mice are placed in an Omnitech Electronics Automated 16 Animal Hot Plate Analgesia Monitor (Columbus, OH; Model AHP16AN) in individual, 9.8 x 7.2 x 15.3 cm (l x w x h) plastic enclosures on top of a
25 copper plate warmed to 55 °C. Infared sensors located near the top of each enclosure record beam crossings that occur as the mice jump off of the heated surface. Latency times for each jump are automatically recorded, and latency to both the first and tenth jumps are used for data analysis. Mice that do not reach the criteria of 10 jumps by 180 seconds are immediately removed from the hotplate to avoid tissue damage, and they are
30 assigned the maximum value of 180 seconds as their latency to tenth jump.

Numerous other animal models of adenosine kinase activity have been described [See, e.g., Davies, et al., Biochem. Pharmacol., 33:347-355 (1984); Keil, et al., Eur. J. Pharmacol., 271:37-46 (1994); Murray, et al., Drug Development Res., 28:410-415 (1993)].

5 Compounds of the present invention were also tested in vitro. The results of some representative studies are shown below in Tables 1 below. The Examples provided before the claims are all adenosine kinase inhibitors. The data indicate that the compounds inhibit adenosine kinase and are useful as adenosine kinase inhibitors. The compounds of the invention including compounds of formula I and II with the variables recited herein are
10 also useful as screening tools or as comparative indicators of adenosine kinase inhibition activity relative to unknown inhibitors or potential inhibitors.

Table 1
Inhibition of Adenosine Kinase by Representative Compounds of the Invention

Compound of Example No.	IC ₅₀ (nM)
6	200
15	7
44	50
53	3
56	35
57	1
64	8
79	5
81	3
100	2
104	2
130	1
133	2
134	1
137	5

147	150
150	150
170	1
175	300
177	25
201	3
205	3
208	4
246	5
247	3
256	1
270	20
272	>100
274	2
283	8
288	0.3
290	1
291	0.6
292	10
303	1
304	1
306	0.3
308	2
309	0.1
315	0.3
319	1
327	1
330	5
333	2

336	8
337	4
338	4.5
347	3
351	4
352	5
353	21
354	11
355	4
356	3
357	12
358	60
359	8
360	50
361	5
362	12
363	28
371	6
403	2
431	2
440	3
441	2
464	6
569	8

Additional compounds of the present invention were tested for adenosine kinase inhibition using the above protocol. These compounds exhibited potent inhibition of adenosine kinase with ED₅₀'s ranging from 1 to 500 nM.

5 Carrageenan hyperalgesia Test-Hotbox Assay

This assay may be indicative of a compound's ability to produce analgesia against carrageenan and capsaicin induced hyperalgesia. The assay is further discussed in Hargreaves K, Dubner R, Brown F, Flores C, Joris J (1988), A new and sensitive method for measuring thermal nociception in cutaneous hyperalgesia. Pain 32: 77-88, hereby fully incorporated by reference.

5 C/D Sprague Dawley rats (Charles River), body weight range 250-350 g, are acclimated in the test room for 30-60 min. before any treatment (habituation). Carrageenan (CARR)(lambda, from Sigma, St. Louis, MO) is dissolved in heated saline at 10 mg/ml. This solution is sonicated and vortexed and then cooled to room temperature.

10 After rats have been habituated they are injected with 100 μ l of the CARR solution into the plantar surface (s.c.) of the right hindpaw. A 26 3/8 g needle is used for injection. The insertion of the needle will start at the midline of the foot between the tori and project toward the heel ~0.25 cm. Needle is then slowly removed from the skin to prevent seepage. Test compounds are administered at a time predetermined in relation to CARR

15 injection (typically 1 hour pre CARR administration). The left hindpaw receives no injections. After carrageenan injection the rats are returned to their cages until 30 minutes before testing at which time they are placed in the Hargreaves thermal stimulator apparatus (Hotbox) for a 30 minute habituation period. Testing (thermal stimulation) is then performed. Each rat is tested 3 times (both right and left hindpaw) with approx. 5

20 minute between trials. The standard setting for the thermal stimulator (voltmeter) is 4.5 and the maximum time of exposure is 20.48 seconds. Scoring is based on latency to withdrawal from the thermal stimuli (0-20.48 seconds). The 2 lowest times of the three taken are averaged and the means are then determined for both the right and left paws (n=6 in most cases). Data is analyzed using GB Stat, with ANOVA protected T-tests to

25 determine significant carrageenan effect (right versus left in same animal) and analgesic effect (right drug treated vs. right control). Results are indicated below as ED₅₀ values in micromolar concentration. For those values in nanomolar concentration, the values are designated by "nm".

30	<u>Compound</u>	<u>ED₅₀ value (micromole/kg)</u>
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	Example 134	0.6
	Example 351	3
	Example 352	3
	Example 353	3
5	Example 354	1
	Example 355	1
	Example 356	1
	Example 357	3
	Example 359	1
10	Example 534	3

Additional compounds of the present invention were tested in the carrageenan and capsaicin induced hyperalgesia hotbox assay using the above protocol in C/D Sprague Dawley rats. These compounds exhibited ED₅₀'s ranging from 1 to >10 micromolar. Compounds exhibiting less potency in the carrageenan hyperalgesia hotbox assay may 15 require a higher dose or potency may be species dependent.

Method of Treating Cerebral Ischemia, Epilepsy,

Nociception (Nociception) (Pain), Inflammation including conditions such as Septic Shock due to Sepsis Infection.

20 In yet another aspect of the present invention a method of treating cerebral ischemia, epilepsy, nociception or nociception, inflammation including conditions such as septic shock due to sepsis infection in a human or lower mammal is disclosed, comprising administering to the mammal a therapeutically effective amount of a compound of formula I with R¹-R⁴ as defined herein. The preferred compounds are those of formula II with the R variables as defined previously. In particular, the present invention relates to a method of treating the above disorders comprising administering a compound of formula II wherein R³ is a substituted aryl or heterocycle moiety wherein the substituent (preferably halogen) is at the meta or 3-position relative to the ring attachment and R⁴ is a substituted heterocycle or aryl moiety wherein the substituent is at the para or 25

4-position relative to the ring attachment. The most preferred use is in the treatment of pain.

Alterations in cellular adenosine kinase activity have been observed in certain disorders. Adenosine kinase activity was found to be decreased, relative to normal liver, 5 in a variety of rat hepatomas: activity of the enzyme giving a negative correlation with tumor growth rate (Jackson, et al., Br. J. Cancer, 1978, 37: 701-713). Adenosine kinase activity was also diminished in regenerating liver after partial hepatectomy in experimental animals (Jackson, et al., Br. J. Cancer, 1978, 37: 701-713). Erythrocyte Adenosine kinase activity was found to be diminished in patients with gout (Nishizawa, et 10 al., Clin. Chim. Acta 1976, 67: 15-20). Lymphocyte adenosine kinase activity was decreased in patients infected with the human immunodeficiency virus (HIV) exhibiting symptoms of AIDS, and increased in asymptomatic HIV-seropositive and HIV- 15 seronegative high-risk subjects, compared to normal healthy controls (Renouf, et al., Clin. Chem. 1989, 35: 1478-1481). It has been suggested that measurement of adenosine kinase activity may prove useful in monitoring the clinical progress of patients with HIV 20 infection (Renouf, et al., Clin. Chem. 1989, 35: 1478-1481). Sepsis infection may lead to a systemic inflammatory syndrome (SIRS), characterized by an increase in cytokine production, neutrophil accumulation, hemodynamic effects, and tissue damage or death. The ability of adenosine kinase inhibitor to elevate adenosine levels in tissues has been 25 demonstrated to ameliorate syndrome symptoms, due to the known anti-inflammatory effects of adenosine. (Firestein, et al., J. of Immunology, 1994: 5853-5859). The ability of adenosine kinase inhibitors to elevate adenosine levels is expected to alleviate pain states, since it has been demonstrated that administration of adenosine or its analogs results in antinociception or antinociception. (Swaynok, et al., Neuroscience, 1989, 32:557-569).

The following Examples illustrate preferred embodiments of the present invention and are not limiting of the specification and claims in any way.

Example 1

30 4-amino-5-(p-dimethylaminophenyl)-7-(p-bromophenyl)pyrido[2,3-d]pyrimidine

A sample of 4-(4-bromophenyl)-3-cyano-6-(4-(dimethylamino)phenyl)pyridine-2-amine (1 g), was suspended in formamide (20 mL), and the reaction was heated to reflux. After about 3 hours, the reaction was complete as monitored by TLC, and the reaction 5 mixture was cooled to room temperature. The product was allowed to precipitate, then recovered by filtration and washed with water. Additional product was recovered from the filtrate. The product was purified by column chromatography eluting with 10% MeOH/CH₂Cl₂ to give the pure title compound. IR (KBr) 3503, 3398, 1731, 1658, 1510, 1467, 1278cm⁻¹; MS m/z 421 (M+H)⁺.

10 The 6-(4-bromophenyl)-3-cyano-4-(4-(dimethylamino)phenyl)pyridine-2-amine compound was prepared as follows:

The reagents, 4-bromoacetophenone (10 mmol, the "R⁴ reagent"), 4-dimethylaminobenzaldehyde (10 mmol, the "R³ reagent"), malononitrile (10 mmol) and ammonium acetate (1.4 g) were added to 25 mL of benzene. The reaction mixture was 15 heated to reflux in a vessel fitted with a Dean-Stork apparatus. After 3.5 hours, the mixture was cooled, and the solvent was removed. The residue was purified by flash chromatography, eluting with methylene chloride, with optional addition of 5% ethyl acetate to the eluant. MS m/z 394 (M+H)⁺.

20

Examples 2-156

Following the procedures of Example 1, except substituting the appropriate reagents for R⁴ and R³ as indicated in Table 2 below, compounds of Examples 2-156 were prepared.

Table 2
Examples 2-156

Ex. No.	Name	R ⁴ Reagent (for 7-position)	R ³ Reagent (for 5-position)	Analytical Data
2	4-amino-5-(4-dimethylaminophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;	1-(4-dimethylamino-phenyl)-ethanone	4-dimethylamino-benzaldehyde	IR (KBr) 3440, 1615, 1760, 1210cm ⁻¹ ; MS m/z 385 (M+H) ⁺ .
3	4-amino-5-(4-methoxyphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;	1-(4-dimethylamino-phenyl)-ethanone	4-methoxybenzaldehyde	IR (KBr) 3330, 1600, 1640, 1780, 1200cm ⁻¹ ; MS m/z 372(M+H) ⁺ .
4	4-amino-5-(4-dimethylaminophenyl)-7-(4-methoxyphenyl)pyrido[2,3-d]pyrimidine;	1-(4-methoxyphenyl)-ethanone	4-dimethylamino-benzaldehyde	IR (KBr) 3660, 1600, 1620, 1510, 1360, 1240 cm ⁻¹ ; MS m/z 372 (M+H) ⁺ .
5	4-amino-5-(4-isopropylphenyl)-7-(4-methoxyphenyl)pyrido[2,3-d]pyrimidine;	1-(4-methoxyphenyl)-ethanone	4-isopropyl-benzaldehyde	IR (KBr) 3430, 3360, 1580, 1540 cm ⁻¹ ; MS m/z 371 (M+H) ⁺ .

6	4-amino-5-(4-neopentylphenyl)-7-(4-methoxyphenyl)pyrido[2,3-d]pyrimidine;	1-(4-methoxyphenyl)-ethanone	4-neopentyl-benzaldehyde	IR (KBr) 3480, 2960, 1580, 1510, 1240 cm ⁻¹ ; MS m/z 399 (M+H) ⁺ .
7	4-amino-5-(4-butoxyphenyl)-7-(4-methoxyphenyl)pyrido[2,3-d]pyrimidine;	1-(4-methoxyphenyl)-ethanone	4-butoxybenzaldehyde	IR (KBr) 3480, 1600, 1580, 1510, 1240, 1180 cm ⁻¹ ; MS m/z 401 (M+H) ⁺ .
8	4-amino-5-(4-methoxyphenyl)-7-(4-bromophenyl)pyrido[2,3-d]pyrimidine;	1-(4-bromophenyl)-ethanone	4-methoxybenzaldehyde	IR (KBr) 3660, 1600, 1680, 1520, 1240 cm ⁻¹ ; MS m/z 407 (M+H) ⁺ .
9	4-amino-5-(4-isopropoxyphenyl)-7-(4-methoxyphenyl)pyrido[2,3-d]pyrimidine;	1-(4-methoxyphenyl)-ethanone	4-isopropoxy-benzaldehyde	IR (KBr) 3480, 2940, 1600, 1580, 1504 cm ⁻¹ ; MS m/z 386 (M+H) ⁺ .
10	4-amino-5-(4-butoxyphenyl)-7-(4-N-formylpiperazinylphenyl)pyrido[2,3-d]pyrimidine;	1-(4-N-formylpiperazinylphenyl)-ethanone	4-butoxy-benzaldehyde	IR (KBr) 3480, 2940, 1660, 1600, 1580, 1510 cm ⁻¹ ; MS m/z 483 (M+H) ⁺ .

11	4-amino-5-(4-benzyloxyphenyl)-7-(4-methoxyphenyl)pyrido[2,3-d]pyrimidine;	1-(4-methoxyphenyl)-ethanone	4-benzyloxy-benzaldehyde	IR (KBr) 3480, 3040, 1600, 1580, 1560 cm ⁻¹ ; MS m/z 435 (M+H) ⁺ .
12	4-amino-5-(4-phenoxyphenyl)-7-(4-methoxyphenyl)pyrido[2,3-d]pyrimidine;	1-(4-methoxyphenyl)-ethanone	4-phenoxy-benzaldehyde	IR (KBr) 3456, 3053, 1580, 1558, 1247 cm ⁻¹ ; MS m/z 421 (M+H) ⁺ .
13	4-amino-5-(4-isopropylphenyl)-7-(4-diethylmalonylallylphenyl)pyrido[2,3-d]pyrimidine;	1-(4-(3-(diethylmalonyl)allyl) phenyl)-ethanone	4-isopropyl-benzaldehyde	IR (KBr) 3480, 2980, 1735, 1580, 1555 cm ⁻¹ ; MS m/z 539 (M+H) ⁺ .
14	4-amino-5-(4-isopropylphenyl)-7-(4-t-butylacrylphenyl)pyrido[2,3-d]pyrimidine;	1-(4-t-butylacrylphenyl)-ethanone	4-isopropyl-benzaldehyde	IR (KBr) 3471, 2957, 1708, 1584, 1556, 1149 cm ⁻¹ ; MS m/z 467 (M+H) ⁺ .
15	4-amino-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;	1-(4-dimethylaminophenyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3480, 1610, 1580, 1560, 1360, 1200 cm ⁻¹ ; MS m/z 421 (M+H) ⁺ .

¹⁶	4-amino-5-(3,4-dimethoxyphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;	1-(4-dimethylaminophenyl)-ethanone	3,4-dimethoxybenzaldehyde	IR (KBr) 3450, 1610, 1580, 1560, 1510 cm ⁻¹ ; MS m/z 402 (M+H) ⁺ .
¹⁷	4-amino-5-(3-t-butylacrylphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;	1-(4-dimethylaminophenyl)-ethanone	3-(3-formylphenyl)acrylic acid t-butyl ester	IR (KBr) 3480, 3400, 1700, 1610, 1580, 1560 cm ⁻¹ ; MS m/z 468 (M+H) ⁺ .
¹⁸	4-amino-5-(3-methoxyphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;	1-(4-dimethylaminophenyl)-ethanone	3-methoxybenzaldehyde	IR (KBr) 3475, 1610, 1580, 1560, 1200 cm ⁻¹ ; MS m/z 372 (M+H) ⁺ .
¹⁹	4-amino-5-(3,5-dimethoxyphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;	1-(4-dimethylaminophenyl)-ethanone	3,5-dimethoxybenzaldehyde	IR (KBr) 3419, 1637, 1600, 1572, 1371, 1202 cm ⁻¹ ; MS m/z 402 (M+H) ⁺ .
²⁰	4-amino-5-(3-diethylmalonylallylphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;	1-(4-dimethylaminophenyl)-ethanone	2-[2-(3-formylphenyl)vinyl]malonic acid diethyl ester	IR (KBr) 3480, 1720, 1610, 1580, 1558, 1524, 1360 cm ⁻¹ ; MS m/z 540 (M+H) ⁺ .

²¹	4-amino-5-(3-vinylpyridinylphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;	1-(4-dimethylaminophenyl)-ethanone	3-vinylpyridinyl-benzaldehyde	IR (KBr) 3480, 1610, 1580, 1560, 1513, 1360 cm ⁻¹ ; MS m/z 385 (M+H) ⁺ .
²²	4-amino-5-(3-trifluoromethylphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;	1-(4-dimethylaminophenyl)-ethanone	3-trifluoromethyl-benzaldehyde	IR (KBr) 3480, 1610, 1580, 1560, 1360, 1200 cm ⁻¹ ; MS m/z 410 (M+H) ⁺ .
²³	4-amino-5-(3-carboxamidophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;	1-(4-dimethylaminophenyl)-ethanone	3-amido-benzaldehyde	IR (KBr) 3480, 1610, 1580, 1380, 1200 cm ⁻¹ ; MS m/z 446 (M+H) ⁺ .
²⁴	4-amino-5-(3-cyanophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;	1-(4-dimethylaminophenyl)-ethanone	3-cyano-benzaldehyde	IR (KBr) 3460, 3400, 2210, 1610, 1580, 1554, 1360 cm ⁻¹ ; MS m/z 367 (M+H) ⁺ .
²⁵	4-amino-5-(3-benzyloxyphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;	1-(4-dimethylaminophenyl)-ethanone	3-benzyloxy-benzaldehyde	IR (KBr) 3470, 1640, 1580, 1550, 1515, 1357, 1250 cm ⁻¹ ; MS m/z 448 (M+H) ⁺ .

26	4-amino-5-(3-methoxyphenyl)-7-(4-methoxyphenyl)pyrido[2,3-d]pyrimidine;	1-(4-methoxyphenyl)-ethanone	3-methoxybenzaldehyde	IR (KBr) 3470, 1640, 1580, 1550, 1515, 1357, 1250, 1240, 1180 cm ⁻¹ ; MS m/z 359 (M+H) ⁺ .
27	4-amino-5-(3-bromophenyl)-7-(4-butoxyphenyl)pyrido[2,3-d]pyrimidine;	1-(4-butoxyphenyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3478, 1610, 1580, 1560, 1515, 1355, 1255, 1240, 1180 cm ⁻¹ ; MS m/z 449 (M+H) ⁺ .
28	4-amino-5-(3-(2-pyridyl)phenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;	1-(4-dimethylaminophenyl)-ethanone	3-(2-pyridyl)-benzaldehyde	IR (microscope) 3476, 1609, 1580, 1560, 1358 cm ⁻¹ ; MS m/z 419 (M+H) ⁺ .
29	4-amino-5-(3-methylphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;	1-(4-dimethylaminophenyl)-ethanone	3-methyl-benzaldehyde	IR (microscope) 3400, 1640, 1600, 1580, 1540 cm ⁻¹ ; MS m/z 356 (M+H) ⁺ .

30	4-amino-5-(3-chlorophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;	1-(4-dimethylaminophenyl)-ethanone	3-chloro-benzaldehyde	IR (microscope) 3400, 1600, 1580, 1540 cm ⁻¹ ; MS m/z 376 (M+H) ⁺ .
31	4-amino-5-(3-fluorophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;	1-(4-dimethylaminophenyl)-ethanone	3-fluoro-benzaldehyde	IR (microscope) 3480, 1640, 1580, 1560 cm ⁻¹ ; MS m/z 360 (M+H) ⁺ .
32	4-amino-5-(3-bromophenyl)-7-(4-methoxyphenyl)pyrido[2,3-d]pyrimidine;	1-(4-methoxyphenyl)-ethanone	3-bromo-benzaldehyde	IR (microscope) 3485, 1607, 1575, 1550, 1515, 1350, 1255, 1240, 1180, 1030 cm ⁻¹ ; MS m/z 407 (M+H) ⁺ .
33	4-amino-5-(3-methoxyphenyl)-7-(4-bromophenyl)pyrido[2,3-d]pyrimidine;	1-(4-bromophenyl)-ethanone	3-methoxy-benzaldehyde	IR (microscope) 3450, 1640, 1573, 1555, 1496, 1350, 1260 cm ⁻¹ ; MS m/z 407 (M+H) ⁺ .

34	4-amino-5-(3-bromophenyl)-7-phenyl pyrido[2,3-d]pyrimidine;	1-phenyl-ethanone	3-bromo-benzaldehyde	IR (KBr) 3480, 1640, 1580, 1560, 1480, 1350, 700 cm ⁻¹ ; MS m/z 377 (M+H) ⁺ .
35	4-amino-5-(3-bromophenyl)-7-(4-ethylphenyl)pyrido[2,3-d]pyrimidine;	1-(4-ethylphenyl)-ethanone	3-bromo-benzaldehyde	IR (microscope) 3480, 1645, 1580 (broad), 1490, 1380 cm ⁻¹ ; MS m/z 405 (M+H) ⁺ .
36	4-amino-5-(3-bromophenyl)-7-(4-bromophenyl)pyrido[2,3-d]pyrimidine;	1-(4-bromophenyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3480, 1610, 1575, 1540, 1350 cm ⁻¹ ; MS m/z 455 (M+H) ⁺ .
37	4-amino-5-(3-bromophenyl)-7-(4-cyanophenyl)pyrido[2,3-d]pyrimidine;	1-(4-cyanophenyl)-ethanone	3-bromo-benzaldehyde	IR (microscope) 3480, 2230, 1618, 1580, 1555, 1545, 1350 cm ⁻¹ ; MS m/z 402 (M+H) ⁺ .

38	4-amino-5-(3-bromophenyl)-7-(4-hydroxyphenyl)pyrido[2,3-d]pyrimidine;	1-(4-hydroxyphenyl)-ethanone	3-bromo-benzaldehyde	IR (microscope) 3481, 3060 (broad), 1645, 1580, 1560, 1544, 1360, 1240 1155 cm ⁻¹ ; MS m/z 393 (M+H) ⁺ .
39	4-amino-5-(3-iodophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;	1-(4-dimethylaminophenyl)-ethanone	3-iodo-benzaldehyde	IR (microscope) 3500, 3040, 1640, 1600, 1580, 1560 cm ⁻¹ ; MS m/z 468 (M+H) ⁺ .
40	4-amino-5-(3-ethoxyphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;	1-(4-dimethylaminophenyl)-ethanone	3-ethoxy-benzaldehyde	IR (microscope) 3460, 3250, 1640, 1600, 1580, 1560 cm ⁻¹ ; MS m/z 386 (M+H) ⁺ .
41	4-amino-5-(3-trifluoromethoxyphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;	1-(4-dimethylaminophenyl)-ethanone	3-trifluoromethoxy-benzaldehyde	IR (microscope) 3480, 1710, 1610, 1580, 1560, 1540 cm ⁻¹ ; MS m/z 426 (M+H) ⁺ .

42	4-amino-5-(3,5-dichlorophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;	1-(4-dimethylaminophenyl)-ethanone	3,5-dichlorobenzaldehyde	IR (microscope) 3500, 3040, 1640, 1600, 1580, 1560 cm ⁻¹ ; MS m/z 411 (M+H) ⁺ .
43	4-amino-5-(3-bromo-4-fluorophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;	1-(4-dimethylaminophenyl)-ethanone	3-bromo-4-fluorobenzaldehyde	IR (microscope) 3440, 3015, 1633, 1607, 1583 cm ⁻¹ ; MS m/z 438 (M+H) ⁺ .
44	4-amino-5-(3-hydroxyphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;	1-(4-dimethylaminophenyl)-ethanone	3-hydroxybenzaldehyde	IR (microscope) 3450, 1640, 1610, 1580, 1560 cm ⁻¹ ; MS m/z 358 (M+H) ⁺ .
45	4-amino-5-(3-bromophenyl)-7-(4-morpholinylphenyl)pyrido[2,3-d]pyrimidine;	1-(4-morpholinylphenyl)-ethanone	3-bromo-benzaldehyde	IR (microscope) 3483, 1607, 1578, 1561, 1518, 1355, 1228 1120 cm ⁻¹ ; MS m/z 462 (M+H) ⁺ .

46	4-amino-5-(3-bromophenyl)-7-(4-piperidinylphenyl)pyrido[2,3-d]pyrimidine;	1-(4-piperidinylphenyl)-ethanone	3-bromo-benzaldehyde	IR (microscope) 3486, 1606, 1561, 1540, 1519, 1353, 1231, 1199, 1128 cm ⁻¹ ; MS m/z 460 (M+H) ⁺ .
47	4-amino-5-(3-bromophenyl)-7-(4-(imidazol-1-yl)phenyl)pyrido[2,3-d]pyrimidine;	1-(4-(imidazol-1-yl)phenyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3481, 1580, 1555, 1525, 1482, 1352, 1303, 1053 cm ⁻¹ ; MS m/z 443 (M+H) ⁺ .
48	4-amino-5-(3-bromophenyl)-7-(4-chlorophenyl)pyrido[2,3-d]pyrimidine;	1-(4-chlorophenyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3470, 1635, 1580, 1560, 1500, 1350, 1090 cm ⁻¹ ; MS m/z 411 (M+H) ⁺ .
49	4-amino-5-(3-bromophenyl)-7-(4-isopropylphenyl)pyrido[2,3-d]pyrimidine;	1-(4-isopropylphenyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3484, 1610, 1579, 1560, 1550, 1483, 1357 cm ⁻¹ ; MS m/z 419 (M+H) ⁺ .

50	4-amino-5-(3-bromophenyl)-7-(4-trifluorophenyl)pyrido[2,3-d]pyrimidine;	1-(4-trifluorophenyl)-ethanone	3-bromo-benzaldehyde	IR (microscope) 3481, 3289, 1616, 1579, 1547, 1324, 1312, 1122, 1070 cm ⁻¹ ; MS m/z 445 (M+H) ⁺ .
51	4-amino-5-(3-bromophenyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine;	1-(4-diethylaminophenyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3481, 1607, 1578, 1561, 1533, 1353, 1200, 1155 cm ⁻¹ ; MS m/z 448 (M+H) ⁺ .
52	4-amino-5-(3-bromophenyl)-7-(3,4,5-trimethoxyphenyl)pyrido[2,3-d]pyrimidine;	1-(3,4,5-trimethoxyphenyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3485, 1579, 1548, 1507, 1340, 1129 cm ⁻¹ ; MS m/z 467 (M+H) ⁺ .
53	4-amino-5-(3-(3-methoxybenzyl)phenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;	1-(4-dimethylaminophenyl)-ethanone	3-(3-methoxybenzyl)-benzaldehyde	IR (KBr) 3425, 1613, 1580, 1558, 1537 cm ⁻¹ ; MS m/z 478 (M+H) ⁺ .

54	4-amino-5-(3-methoxyethoxyphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;	1-(4-dimethylaminophenyl)-ethanone	3-methoxyethoxybenzaldehyde	IR (KBr) 3469, 1610, 1580, 1560, 1357 cm ⁻¹ ; MS m/z 416 (M+H) ⁺ .
55	4-amino-5-(3,4-methylenedioxophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;	1-(4-dimethylaminophenyl)-ethanone	3,4-methylenedioxobenzaldehyde	IR (KBr) 3466, 16245, 1579, 1560 cm ⁻¹ ; MS m/z 386 (M+H) ⁺ .
56	4-amino-5-(3-bromophenyl)-7-(4-ethoxyphenyl)pyrido[2,3-d]pyrimidine;	1-(4-ethoxyphenyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3480, 1607, 1579, 1560, 1517, 1360, 1238, 1180 cm ⁻¹ ; MS m/z 421 (M+H) ⁺ .
57	4-amino-5-(3-bromophenyl)-7-(2'-thiophene)pyrido[2,3-d]pyrimidine;	1-(2-thienyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3470, 1579, 1560, 1547, 1429, 1361 cm ⁻¹ ; MS m/z 383 (M+H) ⁺ .
58	4-amino-5-(3-bromophenyl)-7-(4-fluorophenyl)pyrido[2,3-d]pyrimidine;	1-(4-fluorophenyl)-ethanone	3-bromo-benzaldehyde	IR (microscope) 3476, 1600, 1580, 1555, 1515, 1350, 1230 cm ⁻¹ ; MS m/z 395 (M+H) ⁺ .

59	4-amino-5-(3-dimethylaminophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;	1-(4-dimethylaminophenyl)-ethanone	3-dimethylamino-benzaldehyde	IR (KBr) 3436, 1601, 1580, 1563, 1534, 1200 cm ⁻¹ ; MS m/z 385 (M+H) ⁺ .
60	4-amino-5-phenyl-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;	1-(4-dimethylaminophenyl)-ethanone	benzaldehyde	IR (KBr) 3400, 1600, 1580, 1560, 1530, 1200 cm ⁻¹ ; MS m/z 342 (M+H) ⁺ .
61	4-amino-5-(3,4,5-trimethoxyphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;	1-(4-dimethylaminophenyl)-ethanone	3,4,5-trimethoxy-benzaldehyde	IR (KBr) 33460, 1607, 1578, 1127cm ⁻¹ ; MS m/z 432 (M+H) ⁺ .
62	4-amino-5-(3-bromophenyl)-7-(4-nitrophenyl)pyrido[2,3-d]pyrimidine;	1-(4-nitrophenyl)-ethanone	3-bromo-benzaldehyde	IR (microscope) 3485, 1618, 1580, 1550, 1520, 1340, 860 cm ⁻¹ ; MS m/z 422 (M+H) ⁺ .
63	4-amino-5-(3-bromophenyl)-7-(4-iodophenyl)pyrido[2,3-d]pyrimidine;	1-(4-iodophenyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3480, 1610, 1575, 1570, 1540, 1350, 1000 cm ⁻¹ ; MS m/z 503 (M+H) ⁺ .

64	4-amino-5-(3-bromophenyl)-7-(3,4-methylenedioxyphenyl)pyrido[2,3-d]pyrimidine;	1-(3,4-methylenedioxyphenyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3485, 1607, 1575, 1545, 1500, 1440, 1350, 1255, 1038 cm ⁻¹ ; MS m/z 421 (M+H) ⁺ .
65	4-amino-5-(thiophen-2-yl)-7-(4-morpholinylphenyl)pyrido[2,3-d]pyrimidine;	1-(4-morpholinylphenyl)-ethanone	thiophene-2-carboxaldehyde	IR (KBr) 3480, 1607, 1580, 1560, 1226 cm ⁻¹ ; MS m/z 390 (M+H) ⁺ .
66	4-amino-5-(3,5-dimethoxyphenyl)-7-(thiophen-2-yle)pyrido[2,3-d]pyrimidine;	1-(thiophen-2-yl)-ethanone	3,5-dimethoxy-benzaldehyde	IR (KBr) 3450, 1640, 1600, 1580, 1560 cm ⁻¹ ; MS m/z 365 (M+H) ⁺ .
67	4-amino-5-(3-bromophenyl)-7-(4-carboxamidophenyl)pyrido[2,3-d]pyrimidine;	1-(4-carboxamidophenyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3481, 1674, 1611, 1577, 1558, 1352 cm ⁻¹ ; MS m/z 420 (M+H) ⁺ .

68	4-amino-5-(3-bromophenyl)-7-(4-(2-methoxyethoxyphenyl)pyrido[2,3-d]pyrimidine;	1-(4-(2-methoxyethoxyphenyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3478, 1607, 1580, 1560, 1515, 1357, 1260, 1235, 1180, 1113 cm ⁻¹ ; MS m/z 451 (M+H) ⁺ .
69	4-amino-5-(3,5-dimethoxyphenyl)-7-(4-morpholinylphenyl)pyrido[2,3-d]pyrimidine;	1-(4-morpholinylphenyl)-ethanone	3,5-dimethoxy-benzaldehyde	IR (KBr) 3450, 1608, 1580, 1555, 1541, 1230, 1210, 1160 cm ⁻¹ ; MS m/z 444 (M+H) ⁺ .
70	4-amino-5-(3-trifluoromethylphenyl)-7-(thiophene-2-yl)pyrido[2,3-d]pyrimidine;	1-(thiophene-2-yl)-ethanone	3-trifluoromethyl-benzaldehyde	IR (KBr) 3486, 1620, 1580, 1560, 1325, 1123cm ⁻¹ ; MS m/z 373 (M+H) ⁺ .
71	4-amino-5-(3-bromophenyl)-7-(4-aminophenyl)pyrido[2,3-d]pyrimidine;	1-(4-aminophenyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3450, 1632, 1605, 1580, 1365 cm ⁻¹ ; MS m/z 393 (M+H) ⁺ .

72	4-amino-5-(3-bromo-4-fluorophenyl)-7-(thiophene-2-yl)pyrido[2,3-d]pyrimidine;	1-(thiophene-2-yl)-ethanone	3-bromo-4-fluoro-benzaldehyde	IR (KBr) 3480, 1640, 1580, 1560, 1500cm ⁻¹ ; MS m/z 401 (M+H) ⁺ .
73	4-amino-5-(3-bromo-4-fluorophenyl)-7-(2-furanyl)pyrido[2,3-d]pyrimidine;	1-(2-furanyl)-ethanone	3-bromo-4-fluoro-benzaldehyde	IR (KBr) 3460, 1600, 1580, 1560, 1500cm ⁻¹ ; MS m/z 385 (M+H) ⁺ .
74	4-amino-5-(3,5-dimethoxyphenyl)-7-(4-iodophenyl)pyrido[2,3-d]pyrimidine;	1-(4-iodophenyl)-ethanone	3,5-dimethoxy-benzaldehyde	IR (KBr) 3460, 1604, 1575, 1556, 1541, 1207, 1160 cm ⁻¹ ; MS m/z 485 (M+H) ⁺ .
75	4-amino-5-(3,5-dimethoxyphenyl)-7-(4-imidazolylphenyl)pyrido[2,3-d]pyrimidine;	1-(4-imidazolylphenyl)-ethanone	3,5-dimethoxy-benzaldehyde	IR (KBr) 3459, 1604, 1580, 1556, 1524, 1484, 1304, 1159, 1056 cm ⁻¹ ; MS m/z 425 (M+H) ⁺ .
76	4-amino-5-(3,5-dimethoxyphenyl)-7-(4-(thiophene-2-yl)phenyl)pyrido[2,3-d]pyrimidine;	1-(4-(thiophene-2-yl)phenyl)-ethanone	3,5-dimethoxy-benzaldehyde	IR (KBr) 3457, 1602, 1579, 1557, 1207, 1159 cm ⁻¹ ; MS m/z 441 (M+H) ⁺ .

77	4-amino-5-(3,5-dimethoxyphenyl)-7-(4-(3-pyridyl)phenyl)pyrido[2,3-d]pyrimidine;	1-(4-(3-pyridyl)phenyl)-ethanone	3,5-dimethoxy-benzaldehyde	IR (KBr) 3452, 1604, 1578, 1558, 1287, 1206, 1159 cm ⁻¹ ; MS m/z 436 (M+H) ⁺ .
78	4-amino-5-(3-bromophenyl)-7-(4-(4-methylpiperidinyl)phenyl)pyrido[2,3-d]pyrimidine;	1-(4-(4-methylpiperidinyl)phenyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3475, 1607, 1577, 1558, 1540, 1356, 1232 cm ⁻¹ ; MS m/z 475 (M+H) ⁺ .
79	4-amino-5-(3-bromophenyl)-7-(4-pyrrolidinylphenyl)pyrido[2,3-d]pyrimidine;	1-(4-pyrrolidinylphenyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3486, 1608, 1577, 1560, 1533, 1353, 1196 cm ⁻¹ ; MS m/z 446 (M+H) ⁺ .
80	4-amino-5-(4-bromothiophen-2-yl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;	1-(4-dimethylaminophenyl)-ethanone	4-bromothiophene-2-carboxaldehyde	IR (KBr) 3327, 1604, 1578, 1548, 1521, 1367, 1350, 1202, 820 cm ⁻¹ ; MS m/z 426 (M+H) ⁺ .

81	4-amino-5-(4-bromothiophene-2-yl)-7-(4-morpholinylphenyl)pyrido[2,3-d]pyrimidine;	1-(4-morpholinylphenyl)-ethanone	4-bromothiophene-2-carboxaldehyde	IR (KBr) 3460, 1606, 1578, 1558, 1541, 1517, 1232, 824 cm ⁻¹ ; MS m/z 468 (M+H) ⁺ .
82	4-morpholinyl-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;	1-(4-dimethylaminophenyl)-ethanone	3-bromophenyl-benzaldehyde	IR (microscope) 3340, 1603, 1580, 1540 cm ⁻¹ ; MS m/z 490 (M+H) ⁺ .
83	4-amino-5-(4-(5-bromothiophene-2-yl)phenyl)-7-(4-morpholinylphenyl)pyrido[2,3-d]pyrimidine;	1-(4-morpholinylphenyl)-ethanone	4-(5-bromothiophene-2-yl)-)benzaldehyde	IR (KBr) 3460, 1606, 1580, 1558, 1541, 1517, 1233 cm ⁻¹ ; MS m/z 468 (M+H) ⁺ .
84	4-amino-5-(4-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;	1-(4-dimethylaminophenyl)-ethanone	4-bromo-benzaldehyde	IR (microscope) 3480, 3320, 1603, 1580, 1540, 820 cm ⁻¹ ; MS m/z 420 (M+H) ⁺ .
85	4-amino-5-(3-bromophenyl)-7-(4-(acetylamino)phenyl)pyrido[2,3-d]pyrimidine;	1-(4-(acetylamino)phenyl)-ethanone	3-bromo-benzaldehyde	IR (microscope) 3480 1600, 1580, 1520cm ⁻¹ ; MS m/z 434 (M+H) ⁺ .

86	4-amino-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;	1-(4-dimethylaminophenyl)-ethanone	3-bromo-benzaldehyde	IR (microscope) 3300, 1606, 1600, 1580, 1560 cm ⁻¹ ; MS m/z 421 (M+H) ⁺ .
87	4-amino-5-(3,5-dimethoxyphenyl)-7-(5-pyrimidinylphenyl)pyrido[2,3-d]pyrimidine;	1-(5-pyrimidinylphenyl)-ethanone	3,5-dimethoxy-benzaldehyde	IR (microscope) 3458, 1602, 1579, 1558, 1460, 1414, 1364, 1196, 1058 cm ⁻¹ ; MS m/z 437 (M+H) ⁺ .
88	4-(4-fluorophenyl)amino)-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;	1-(4-dimethylaminophenyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3410, 1605, 1570, 1525, 1503 cm ⁻¹ ; MS m/z 514 (M+H) ⁺ .
89	4-amino-5-(4-bromothiophene-2-yl)-7-(4-pyrrolidinylphenyl)pyrido[2,3-d]pyrimidine;	1-(4-pyrrolidinylphenyl)-ethanone	4-bromothiophene-2-carboxaldehyde	IR (KBr) 3470, 1609, 1577, 1555, 1520, 1409, 1386, 1350, 1196, 821 cm ⁻¹ ; MS m/z 452 (M+H) ⁺ .

90	4-amino-5-(4-bromothiophene-2-yl)-7-(thiophene-2-yl)pyrido[2,3-d]pyrimidine;	1-(thiophene-2-yl)-ethanone	4-bromothiophene-2-carboxaldehyde	IR (KBr) 3308, 1606, 1578, 1543, 1526, 1427, 1359 cm ⁻¹ ; MS m/z 389 (M+H) ⁺ .
91	4-amino-5-(3-bromophenyl)-7-(5-(dimethylamino)thiophene-2-yl)pyrido[2,3-d]pyrimidine;	1-(5-(dimethylamino)thiophene-2-yl)-ethanone	3-bromo-benzaldehyde	IR (microscope) 3490, 1581, 1556, 1501, 1481, 1407, 1373, 1072 cm ⁻¹ ; MS m/z 426 (M+H) ⁺ .
92	4-amino-5-(3-bromo-5-iodophenyl)-7-(4-(dimethylamino)phenyl)pyrido[2,3-d]pyrimidine;	1-(4-(dimethylamino)phenyl)-ethanone	3-bromo-5-iodobenzaldehyde	IR (KBr) 3493, 1608, 1562, 1533, 1364, 1350, 1200 cm ⁻¹ ; MS m/z 546 (M+H) ⁺ .
93	4-amino-5-(3,5-di(trifluoromethyl)phenyl)-7-(4-(dimethylamino)phenyl)pyrido[2,3-d]pyrimidine;	1-(4-(dimethylamino)phenyl)-ethanone	3,5-di(trifluoromethyl)-benzaldehyde	IR (KBr) 3484, 1607, 1580, 1554, 1386, 1280 cm ⁻¹ ; MS m/z 478 (M+H) ⁺ .

94	4-amino-5-(3,5-di(trifluoromethyl)phenyl)-7-(4-morpholinylphenyl)pyrido[2,3-d]pyrimidine;	1-(4-morpholinylphenyl)-ethanone	3,5-di(trifluoromethyl)-benzaldehyde	IR (KBr) 3500, 1643, 1602, 1578, 1554, 1280 cm ⁻¹ ; MS m/z 520 (M+H) ⁺ .
95	4-amino-5-(3,5-dibromophenyl)-7-(4-(dimethylamino)phenyl)pyrido[2,3-d]pyrimidine;	1-(4-(dimethylamino)phenyl)-ethanone	3,5-dibromo-benzaldehyde	IR (KBr) 3440, 1608, 1570, 1559, 1536 cm ⁻¹ ; MS m/z 498 (M+H) ⁺ .
96	4-amino-5-(3,5-dibromophenyl)-7-(4-morpholinylphenyl)pyrido[2,3-d]pyrimidine;	1-(4-morpholinylphenyl)-ethanone	3,5-dibromo-benzaldehyde	IR (KBr) 3480, 1607, 1560, 1540, 1225 cm ⁻¹ ; MS m/z 540 (M+H) ⁺ .
97	4-amino-5-(4-bromothiophene-2-yl)-7-(4-(4-methylpiperidinyl)phenyl)pyrido[2,3-d]pyrimidine;	1-(4-(4-methylpiperidinyl)phenyl)-ethanone	4-bromothiophene-2-carboxaldehyde	IR (KBr) 3460, 1608, 1576, 1557, 1540, 1513, 1384, 1353, 1240, 823 cm ⁻¹ ; MS m/z 481 (M+H) ⁺ .
98	4-amino-5-(3,5-dibromophenyl)-7-(4-(dimethylamino)phenyl)pyrido[2,3-d]pyrimidine;	1-(4-(dimethylamino)phenyl)-ethanone	3,5-dibromo-benzaldehyde	IR (KBr) 3486, 1608, 1570, 1559, 1536, 1360, 1350, 1200, 823 cm ⁻¹ ; MS m/z 498 (M+H) ⁺ .

99	4-amino-5-(3-bromophenyl)-7-(3-(dimethylamino)phenyl)pyrido[2,3-d]pyrimidine;	1-(4-(dimethylamino)phenyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3480, 1601, 1579, 1548, 1483, 1357 cm ⁻¹ ; MS m/z 420 (M+H) ⁺ .
100	4-amino-5-(3-bromophenyl)-7-(4-methylsulfonylphenyl)pyrido[2,3-d]pyrimidine;	1-(4-methylsulfonylphe-nyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3486, 1600, 1580, 1550, 1490 cm ⁻¹ ; MS m/z 455 (M+H) ⁺ .
101	4-amino-5-(3-bromophenyl)-7-(3-methoxyphenyl)pyrido[2,3-d]pyrimidine;	1-(3-methoxyphenyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3486, 1605, 1578, 1550, 1492, 1346, 1263 cm ⁻¹ ; MS m/z 407 (M+H) ⁺ .
102	4-amino-5-(3-bromophenyl)-7-(4-(methylthio)phenyl)pyrido[2,3-d]pyrimidine;	1-(4-(methylthio)phenyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3485, 1607, 1578, 1566, 1538, 1350, 1094, 795 cm ⁻¹ ; MS m/z 423 (M+H) ⁺ .
103	4-amino-5-(3-bromophenyl)-7-(3,4-dichlorophenyl)pyrido[2,3-d]pyrimidine;	1-(3,4-dichlorophenyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3482, 1634, 1576, 1545, 1488, 1342 cm ⁻¹ ; MS m/z 445 (M+H) ⁺ .

104	4-amino-5-(3-bromophenyl)-7-(4-(N-methyl-N-formylamino)phenyl)pyrido[2,3-d]pyrimidine;	1-(4-(N-methyl-N-formylamino)phenyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3478, 1672, 1639, 1603, 1579, 1547, 841 cm ⁻¹ ; MS m/z 434 (M+H) ⁺ .
105	4-amino-5-(3-bromophenyl)-7-(4-methylaminophenyl)pyrido[2,3-d]pyrimidine;	1-(4-methylaminophenyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3488, 1637, 1607, 1587, 1360 cm ⁻¹ ; MS m/z 480 (M+H) ⁺ .
106	4-amino-5-(3-bromo-4-fluorophenyl)-7-(4-methylsulfonylphenyl)pyrido[2,3-d]pyrimidine;	1-(4-methylsulfonylphenyl)-ethanone	3-bromo-4-fluoro-benzaldehyde	IR (KBr) 3489, 1578, 1560, 1496, 1311, 1151, 775 cm ⁻¹ ; MS m/z 473 (M+H) ⁺ .
107	4-amino-5-(3-bromophenyl)-7-(3-amino-4-methoxyphenyl)pyrido[2,3-d]pyrimidine;	1-(3-amino-4-methoxyphenyl)-ethanone	3-bromo-benzaldehyde	IR (microscope) 3431, 1629, 1606, 1583, 1274 cm ⁻¹ ; MS m/z 422 (M+H) ⁺ .
108	4-amino-5-(3-bromophenyl)-7-(3-bromo-4-(dimethylamino)phenyl)pyrido[2,3-d]pyrimidine;	1-(3-bromo-4-(dimethylamino)phenyl)-ethanone	3-bromo-benzaldehyde	IR (microscope) 3470, 1638, 1570, 1560, 1538, 1480, 1345 cm ⁻¹ ; MS m/z 498 (M+H) ⁺ .

109	4-amino-5-(3-bromophenyl)-7-(3-methyl-4-(dimethylamino)phenyl)pyrido[2,3-d]pyrimidine;	1-(3-methyl-4-(dimethylamino)phenyl)-ethanone	3-bromo-benzaldehyde	IR (microscope) 3438, 1640, 1605, 1580, 1555, 1368 cm ⁻¹ ; MS m/z 434 (M+H) ⁺ .
110	4-amino-5-(3-bromophenyl)-7-(4-(N-methyl-N-trifluoroacetyl amino)phenyl)pyrido[2,3-d]pyrimidine;	1-(4-(N-methyl-N-trifluoroacetyl amino)phenyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3443, 1699, 1635, 1606, 1201 cm ⁻¹ ; MS m/z 502 (M+H) ⁺ .
111	4-amino-5-(3-bromophenyl)-7-(4-(dimethylamino)-3-fluorophenyl)pyrido[2,3-d]pyrimidine;	1-(4-(dimethylamino)-3-fluorophenyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3438, 1638, 1592, 1365 cm ⁻¹ ; MS m/z 438 (M+H) ⁺ .
112	4-amino-5-(3-bromophenyl)-7-(4-(N-ethyl-N-formylamino)phenyl)pyrido[2,3-d]pyrimidine;	1-(4-(N-ethyl-N-formylamino)phenyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3477, 1672, 1604, 1580, 1562, 1353 cm ⁻¹ ; MS m/z 448 (M+H) ⁺ .
113	4,4-bis(acetylamino)-5-(3-bromophenyl)-7-(4-(N-methyl-N-acetyl amino)phenyl)pyrido[2,3-d]pyrimidine;	1-(4-(N-methyl-N-acetyl amino)phenyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3434, 1667, 1635, 1600, 1200 cm ⁻¹ ; MS m/z 532 (M+H) ⁺ .

114	4-amino-5-(3-bromophenyl)-7-(4-(N-acetyl-N-methylamino)phenyl)pyrido[2,3-d]pyrimidine;	1-(4-(N-acetyl-N-methylamino)phenyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3443, 1667, 1635, 1600, 1200 cm ⁻¹ ; MS m/z 532 (M+H) ⁺ .
115	4-amino-5-(3-bromophenyl)-7-(4-(N-ethylamino)phenyl)pyrido[2,3-d]pyrimidine;	1-(4-(N-ethylamino)phenyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3441, 1633, 1603, 1572, 1368 cm ⁻¹ ; MS m/z 420 (M+H) ⁺ .
116	4-amino-5-(3-bromophenyl)-7-(4-(N-methyl-N-(2-methoxyethyl)amino)phenyl)pyrido[2,3-d]pyrimidine;	1-(N-methyl-N-(2-methoxyethyl)amino)phenyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3439, 1636, 1601, 1529, 1361 cm ⁻¹ ; MS m/z 464 (M+H) ⁺ .
117	4-amino-5-(3-bromophenyl)-7-(4-(N-isopropylamino)phenyl)pyrido[2,3-d]pyrimidine;	1-(N-isopropylamino)phenyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3430, 1632, 1600, 1578, 1530, 1357 cm ⁻¹ ; MS m/z 434 (M+H) ⁺ .
118	4-amino-5-(3-bromophenyl)-7-(4-N-ethyl-N-(2-methoxyethyl)amino)phenyl)pyrido[2,3-d]pyrimidine;	1-(4-N-ethyl-N-(2-methoxyethyl)amino)phenyl)-ethanone	3-bromo-benzaldehyde	IR (microscope) 3488, 1657, 1604, 1579, 1552, 1118 cm ⁻¹ ; MS m/z 506 (M+H) ⁺ .

119	4-amino-5-(3-bromophenyl)-7-(4-N-(3-methoxypropionyl)-N-isopropyl-amino)phenyl)pyrido[2,3-d]pyrimidine;	1-(4-N-(3-methoxypropionyl)-N-isopropyl-amino)phenyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3201, 1679, 1617, 1597, 1576, 1539, 1177, 1117 cm ⁻¹ ; MS m/z 521 (M+H) ⁺ .
120	4-amino-5-(3-bromophenyl)-7-(4-N-(2-(dimethylamino)ethyl)-N-formylamino)phenyl)pyrido[2,3-d]pyrimidine;	1-(4-N-(2-(dimethylamino)ethyl)-N-formylamino)phenyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3475, 1681, 1579, 1351, cm ⁻¹ ; MS m/z 491 (M+H) ⁺ .
121	4-amino-5-(3-bromophenyl)-7-(4-(N-(2-(dimethylamino)ethyl)amino)phenyl)pyrido[2,3-d]pyrimidine;	1-(4-(N-(2-(dimethylamino)ethyl)amino)phenyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3431, 1634, 1601, 1573, 1359 cm ⁻¹ ; MS m/z 463 (M+H) ⁺ .
122	4-amino-5-(3-bromophenyl)-7-(4-(N-methyl-N-(2-cyanoethyl)amino)phenyl)pyrido[2,3-d]pyrimidine;	1-(4-(N-methyl-N-(2-cyanoethyl)amino)phenyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3475, 2220, 1660, 1604, 1580, 1560, 1352 cm ⁻¹ ; MS m/z 459 (M+H) ⁺ .
123	4-amino-5-(3-bromophenyl)-7-(4-(N-methyl-N-(3-methoxypropionyl)amino)phenyl)pyrido[2,3-d]pyrimidine;	1-(4-(N-methyl-N-(3-methoxypropionyl)amino)phenyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3475, 1663, 1604, 1578, 1559, 1352 1114 cm ⁻¹ ; MS m/z 478 (M+H) ⁺ .

124	4-amino-5-(3-bromophenyl)-7-(3-methyl-4-(N-formyl-N-methylamino)phenyl)pyrido[2,3-d]pyrimidine;	1-(3-methyl-4-(N-formyl-N-methylamino)phenyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3486, 1677, 1607, 1579, 1549, 1351 cm ⁻¹ ; MS m/z 448 (M+H) ⁺ .
125	4-amino-5-(3-bromophenyl)-7-(3-methyl-4-(N-methylamino)phenyl)pyrido[2,3-d]pyrimidine;	1-(3-methyl-4-(N-methylamino)phenyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3433, 1635, 1605, 1585, 1359 cm ⁻¹ ; MS m/z 420 (M+H) ⁺ .
126	4-amino-5-(3-bromophenyl)-7-(4-(4-methoxy-2-butyl)phenyl)pyrido[2,3-d]pyrimidine;	1-(4-(4-methoxy-2-butyl)phenyl)-ethanone	3-bromo-benzaldehyde	IR (microscope) 3473, 3063, 1710, 1671, 1582, 1564, 1352 cm ⁻¹ ; MS m/z 593 (M+H) ⁺ .
127	4-amino-5-(3-bromophenyl)-7-(4-(N-methyl-N-(2-(N-phthalimidyl)acetyl)amino)phenyl)pyrido[2,3-d]pyrimidine;	1-(4-(N-methyl-N-(2-(N-phthalimidyl)acetyl)amino)phenyl)-ethanone	3-bromo-benzaldehyde	IR (microscope) 3443, 1638, 1606, 1582, 1359 cm ⁻¹ ; MS m/z 463 (M+H) ⁺ .

128	4-amino-5-(3-bromophenyl)-7-(3-methyl-4-(N-methyl-N-(trifluoroacetyl)amino)phenyl)pyrido[2,3-d]pyrimidine;	1-(3-methyl-4-(N-methyl-N-(trifluoroacetyl)amino)phenyl)-ethanone	3-bromo-benzaldehyde	IR (microscope) 3484, 1701, 1610, 1579, 1559, 1221, 1205, 1151 cm ⁻¹ ; MS m/z 516 (M+H) ⁺ .
129	4-amino-5-(3-bromophenyl)-7-(3-methyl-4-(N-acetyl-N-methylamino)phenyl)pyrido[2,3-d]pyrimidine;	1-(3-methyl-4-(N-acetyl-N-methylamino)phenyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3484, 1663, 1607, 1574, 1547, 1354 cm ⁻¹ ; MS m/z 462 (M+H) ⁺ .
130	4-amino-5-(3-bromophenyl)-7-(6-dimethylamino-3-pyridinyl)pyrido[2,3-d]pyrimidine;	1-(6-dimethylamino-3-pyridinyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3428, 1652, 1635, 1606, 1585, 1365 cm ⁻¹ ; MS m/z 421 (M+H) ⁺ .
131	4-amino-5-(3-cyanophenyl)-7-(4-methylsulfonylphenyl)pyrido[2,3-d]pyrimidine;	1-(4-methylsulfonylphenyl)-ethanone	3-cyano-benzaldehyde	IR (KBr) 3479, 1638, 1576, 1559, 1303, 1147 cm ⁻¹ ; MS m/z 402 (M+H) ⁺ .

132	4-amino-5-(3-cyanophenyl)-7-(4-(N-methyl-N-formylamino)-phenyl)pyrido[2,3-d]pyrimidine;	1-(4-(N-methyl-N-formylamino)-phenyl)-ethanone	3-cyanobenzaldehyde	IR (KBr) 3418, 2230, 1688, 1674, 1584, 1554, 1114 cm ⁻¹ ; MS m/z 381 (M+H) ⁺ .
133	4-amino-5-(3-bromophenyl)-7-(6-(N-methyl-N-formylamino)-3-pyridinyl)pyrido[2,3-d]pyrimidine;	1-(6-(N-methyl-N-formylamino)-3-pyridinyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3474, 1676, 1577, 1561, 1353, 1130cm ⁻¹ ; MS m/z 435 (M+H) ⁺ .
134	4-amino-5-(3-bromophenyl)-7-(6-morpholinyl-3-pyridinyl)pyrido[2,3-d]pyrimidine;	1-(6-morpholinyl-3-pyridinyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3487, 3396, 1601, 1580, 1558, 1234cm ⁻¹ ; MS m/z 463 (M+H) ⁺ .
135	4-amino-5-(3-bromophenyl)-7-(6-(N-methyl-N-methoxyethylamino)-3-pyridinyl)pyrido[2,3-d]pyrimidine;	1-(6-(N-methyl-N-methoxyethylamino)-3-pyridinyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3476, 3307, 1702, 1683, 1605, 1560, 1116cm ⁻¹ ; MS m/z 465 (M+H) ⁺ .
136	4-amino-5-(3-bromophenyl)-7-(6-pyrrolidinyl-3-pyridinyl)pyrido[2,3-d]pyrimidine;	1-(6-pyrrolidinyl-3-pyridinyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3487, 3396, 1601, 1580, 1558, 1234 cm ⁻¹ ; MS m/z 447 (M+H) ⁺ .

137	4-amino-5-(3-bromophenyl)-7-(2-(dimethylamino)-5-pyrimidinyl)pyrido[2,3-d]pyrimidine;	1-(2-(dimethylamino)-5-pyrimidinyl)-ethanone	3-bromo-benzaldehyde	IR (microscope) 3442, 1640, 1604, 1577, 1536, 1408, 1367, 1348 cm ⁻¹ ; MS m/z 422 (M+H) ⁺ .
138	4-amino-5-(3-bromophenyl)-7-(2-(N-methoxyethyl-N-methyl amino)-5-pyrimidinyl)pyrido[2,3-d]pyrimidine;	1-(2-(N-methoxyethyl-N-methyl amino)-5-pyrimidinyl)-ethanone	3-bromo-benzaldehyde	IR (microscope) 3439, 1640, 1606, 1587, 1556, 1537, 1374, 1347 cm ⁻¹ ; MS m/z 466 (M+H) ⁺ .
139	4-amino-5-(3-bromophenyl)-7-(2-(N-formyl-N-methyl amino)-5-pyrimidinyl)pyrido[2,3-d]pyrimidine;	1-(2-(N-formyl-N-methyl amino)-5-pyrimidinyl)-ethanone	3-bromo-benzaldehyde	IR (microscope) 3472, 1687, 1583, 1565, 1459, 1353, 1142, 988 cm ⁻¹ ; MS m/z 436 (M+H) ⁺ .
140	4-amino-5-(3-bromophenyl)-7-(2-(N-methylamino)-5-pyrimidinyl)pyrido[2,3-d]pyrimidine;	1-(2-(N-methylamino)-5-pyrimidinyl)-ethanone	3-bromo-benzaldehyde	IR (microscope) 3483, 1605, 1550, 1346 cm ⁻¹ ; MS m/z 408 (M+H) ⁺ .

141	4-amino-5-(3-bromophenyl)-7-(2-(1-pyrrolidinyl)-5-pyrimidinyl)pyrido[2,3-d]pyrimidine;	1-(2-pyrrolidinyl-5-pyrimidinyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3468, 1600, 1581, 1552, 1527, 1482, 1330 cm ⁻¹ ; MS m/z 448 (M+H) ⁺ .
142	4-amino-5-(3-bromophenyl)-7-(2-(1-morpholinyl)-5-pyrimidinyl)pyrido[2,3-d]pyrimidine;	1-(2-morpholinyl-5-pyrimidinyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3434, 1637, 1608, 1585, 1335, cm ⁻¹ ; MS m/z 463 (M+H) ⁺ .
143	4-amino-5-(3-bromophenyl)-7-(6-(2-oxo-3-oxazolidinyl)-3-pyridinyl)pyrido[2,3-d]pyrimidine;	1-(6-(2-oxo-3-oxazolidinyl)-3-pyridinyl)-ethanone	3-bromo-benzaldehyde	IR (microscope) 3473, 1762, 1583, 1571, 1562, 1491, 1477, 1402, 1348, 1217 cm ⁻¹ ; MS m/z 463 (M+H) ⁺ .
144	4-amino-5-(3-bromophenyl)-7-(2-pyridyl)pyrido[2,3-d]pyrimidine;	1-(2-pyridyl)-ethanone	3-bromo-benzaldehyde	IR (microscope) 3427, 3017, 1601, 783 cm ⁻¹ ; MS m/z 351/353 (M+H) ⁺ .
145	4-amino-5-(3-bromophenyl)-7-(3-pyridyl)pyrido[2,3-d]pyrimidine;	1-(3-pyridyl)-ethanone	3-bromo-benzaldehyde	IR (microscope) 3434, 3042, 1634, 1372 cm ⁻¹ ; MS m/z 351/353 (M+H) ⁺ .

146	4-amino-5-(3-(thiophen-2-yl)phenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;	1-(4-dimethylaminophenyl)-ethanone	3-(thiophen-2-yl)-benzaldehyde	IR (microscope) 3482, 2922, 1578, 1356 cm ⁻¹ ; MS m/z 420/422 (M+H) ⁺ .
147	4-amino-5-(3-(furan-2-yl)phenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;	1-(4-dimethylaminophenyl)-ethanone	3-(furan-2-yl)-benzaldehyde	IR (microscope) 3479, 3104, 1559, 1356 cm ⁻¹ ; MS m/z 420/422 (M+H) ⁺ .
148	4-amino-5-(3-(3-methoxyphenyl)phenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;	1-(4-dimethylaminophenyl)-ethanone	3-(3-methoxyphenyl)-benzaldehyde	IR (microscope) 3477, 2924, 1579, 1356 cm ⁻¹ ; MS m/z 420/422 (M+H) ⁺ .
149	4-amino-5-phenyl-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;	1-(4-dimethylaminophenyl)-ethanone	benzaldehyde	IR (microscope) 3477, 3298, 1580, 1355 cm ⁻¹ ; MS m/z 315 (M+H) ⁺ .
150	4-amino-5-(3-chlorophenyl)-7-(4-(morpholinyl)phenyl)pyrido[2,3-d]pyrimidine;	1-(4-(morpholinyl)phenyl)-ethanone	3-chloro-benzaldehyde	IR (microscope) 3480, 3056, 1579, 1356 cm ⁻¹ ; MS m/z 391 (M+H) ⁺ .
151	4-amino-5-(3-bromo-4-fluorophenyl)-7-(4-(morpholinyl)phenyl)pyrido[2,3-d]pyrimidine;	1-(4-(morpholinyl)phenyl)-ethanone	3-bromo-4-fluoro-benzaldehyde	IR (microscope) 3491, 3044, 1560, 1230 cm ⁻¹ ; MS m/z 453 (M+H) ⁺ .

152	4-amino-5-(3-chlorophenyl)-7-(4-iodophenyl)pyrido[2,3-d]pyrimidine;	1-(4-iodophenyl)-ethanone	3-chloro-benzaldehyde	IR (microscope) 3478, 3280, 1539, 1350 cm ⁻¹ ; MS m/z 432 (M+H) ⁺ .
153	4-amino-5-(3-chlorophenyl)-7-(4-(thiophen-2-yl)phenyl)pyrido[2,3-d]pyrimidine;	1-(4-(thiophen-2-yl)phenyl)-ethanone	3-chloro-benzaldehyde	IR (microscope) 3484, 3055, 1560, 1354 cm ⁻¹ ; MS m/z 459 (M+H) ⁺ .
154	4-amino-5-(3-chlorophenyl)-7-(4-(5-pyrimidinyl)phenyl)pyrido[2,3-d]pyrimidine;	1-(4-(5-pyrimidinyl)phenyl)-ethanone	3-chloro-benzaldehyde	IR (microscope) 3477, 3040, 1578, 1351 cm ⁻¹ ; MS m/z 459 (M+H) ⁺ .
155	4-amino-5-(3-bromo-4-fluorophenyl)-7-(4-iodophenyl)pyrido[2,3-d]pyrimidine;	1-(4-iodophenyl)-ethanone	3-bromo-4-fluoro-benzaldehyde	IR (microscope) 3444, 3048, 1607, 1356 cm ⁻¹ ; MS m/z 494/496 (M+H) ⁺ .
156	4-amino-5-(4-bromothiophene-2-yl)-7-(4-methoxyphenyl)pyrido[2,3-d]pyrimidine;	1-(4-methoxyphenyl)-ethanone	4-bromothiophene-2-carboxaldehyde	IR (microscope) 3460, 3300, 2900-3100, 1700, 1580, 1510 cm ⁻¹ ; MS m/z 413 (M+H) ⁺ .

Example 157

4-amino-5-(3-bromophenyl)methyl-7-(4-(dimethylamino)phenyl)pyrido[2,3-d]pyrimidine hydrochloride

A mixture of 3-cyano-4-(3-bromophenyl)methyl-6-(4-(dimethylamino)phenyl)pyridine-2-amine (1.58 g) and ammonium sulfate (40 mg) in triethyl orthoformate was heated at reflux for 2 hours. The reaction mixture was cooled and added to a mixture of 8 g of ammonia in 150 mL of ethanol. After 16 hours at 25 °C, the reaction was heated at reflux for two hours, and the solvent was removed in vacuo. The residue was purified by chromatography, then converted to the hydrochloride salt by treatment with ether/HCl, followed by drying to give the title compound.

The 3-cyano-4-(3-bromophenyl)methyl-6-(4-(dimethylamino)phenyl)pyridine-2-amine was prepared by a four-step procedure as follows:

step 157a: preparation of 3-bromophenylacetaldehyde (the "R³ reagent")

To a solution of ethyl 3-bromophenylacetate (10.2 g, US patent 2,624,731 (1950)) in 230 mL of dichloromethane was added 42 mL of 1M Dibal-H in toluene at -78 °C with stirring. After 40 minutes at -78 °C, 10 mL of methanol was added, and the reaction allowed to warm to room temperature and partitioned between 50 mL of dichloromethane and 1200 mL of saturated aqueous potassium sodium tartrate. The organic layer was dried over sodium sulfate and the aldehyde used immediately in the next step without purification.

step 157b: preparation of α -(triphenylphosphonium)-4-(dimethylamino)phenylethan-1-one chloride

Following the procedure of Fukui et al. (J. Org. Chem. 33: 3594-3507 (1968)), α -bromo-(4-dimethylaminophenyl)ethan-1-one (the "R⁴ reagent", CAS #37904-72-6; Chem. Abst. (1956), 864) was treated with triphenylphosphine in triethylamine and acetonitrile. The α -bromo-(4-dimethylaminophenyl)ethan-1-one was prepared by bromination with bromine in hydrobromic acid according to the method of Suzuki et al (J. Pharm. Soc.

Japan, (1955), 75:54. Removal of solvent and recrystallization from methanol/ethyl acetate/toluene gave the title product as a white powder.

step 157c: preparation of 1-(4-(dimethylamino)phenyl)-4-(3-bromophenyl)-but-2-en-1-one

5 20 g of α -(triphenylphosphonium)-4-(dimethylamino)phenylethan-1-one chloride (from step b) was partitioned between dichloromethane and 50 mL of 2N NaOH. The organic phase was dried over sodium sulfate and concentrated in vacuo. The residue was mixed with 3-bromophenylacetaldehyde (from step a) for 24 hours at 25 °C. The mixture was purified by chromatography to give 8.35 g (61%) of a cis/trans mixture of the title 10 compound. The cis/trans mixture was taken to the next step without separation of the isomers.

step 157d: preparation of 3-cyano-4-(3-bromophenyl)methyl-6-(4-(dimethyl)aminophenyl)pyridine-2-amine

15 A mixture of 1-(4-(dimethylamino)phenyl)-4-(3-bromophenyl)-but-2-en-1-one chloride (3.85 g, from step c), ammonium acetate (2.6 g) and malononitrile (739 mg) in 3 mL of dimethoxyethane and 22 mL of ethanol was heated at 115 °C for 5 hours, then cooled and worked up by partitioning between dichloromethane and water. The residue obtained on concentration of the organic phase was purified by flash chromatography to 20 give the title compound.

Examples 158-174

Following the procedures of Example 157, except substituting the appropriate reagents for the R⁴ and R³ reagents of Example 157 as indicated in Table 3 below, 25 compounds of Examples 158-174 were prepared. The treatment with aqueous HCl was omitted, and the free bases were obtained except as indicated.

In Examples 167-174, the formamide or formamidine acetate (added periodically until the reaction was complete) treatment was replaced by treatment with triethyl 30 orthoformate at reflux in the presence of a catalytic amount of ammonium sulfate, followed by cooling to 25 °C and addition of excess ammonia in ethanol. After 24 hours,

the precipitated amidine compound was filtered and washed with hexanes, then dried under vacuum. The amidine compound was then heated in 1,2-dichlorobenzene at 120-180 °C for 1-8 hours. The reaction mixture was cooled to room temperature and purified by chromatography, and the product was recrystallized if necessary (chloroform in 5 methanol).

10

Table 3
Examples 158-187

Ex. No.	Name	R ⁴ Reagent (for 7-position)	R ⁵ Reagent (for 5-position)	Analytical Data
158	4-amino-5-(2-phenylethyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine	1-(4-diethylaminophenyl)-ethanone	3-phenyl-propionaldehyde	IR (KBr) 3340,3240-2800,1600,1580,1540; H. Res. MS m/z 398.2343 (M+H) ⁺ .
159	4-amino-5-(2-methylpropyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine	1-(4-diethylaminophenyl)-ethanone	3-methyl-butanaldehyde	IR (KBr) 3550,3410,3320,3240-2800,1605,1580,1560 H. Res. MS m/z 350.2357 (M+H) ⁺ .
160	4-amino-5-(butyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine	1-(4-diethylaminophenyl)-ethanone	pentanaldehyde	IR (KBr) 3450,3300,3200-2800,1660,1610,1580,1540 H. Res. MS m/z 350.2354 (M+H) ⁺ .

161	4-amino-5-(2-(4-bromophenyl)ethyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine	1-(4-diethylaminophenyl)-ethanone	4-(4-bromophenyl)-propionaldehyde	IR (KBr) 3500,3300,3200-3000,1650,1615,1580 H. Res. MS m/z 478.1429 (M+H) ⁺ .
162	4-amino-5-(butyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine	1-(4-dimethylaminophenyl)-ethanone	pentanal	IR (KBr) 3400,3350,3200-2900,1650,1620,1580,1570 H. Res. MS m/z 322.2032 (M+H) ⁺ .
163	4-amino-5-(2-(3-cyanophenyl)methyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine	1-(4-dimethylaminophenyl)-ethanone	3-cyanophenyl-acetaldehyde	IR (KBr) 2850-3550,2220,1610,1580,1560,1540 MS m/z 381 (M+H) ⁺ .
164	4-amino-5-(2-(N-carbobenzyloxy)aminooethyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine	1-(4-dimethylaminophenyl)-ethanone	3-(N-carbobenzyloxy)-aminopropionaldehyde	IR (KBr) 3000-3500,1710,1690,1650,1590 H. Res. MS m/z 443.2184 (M+H) ⁺ .
165	4-amino-5-(cycloheptyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine	1-(4-dimethylaminophenyl)-ethanone	cycloheptane-carboxaldehyde	IR (KBr) 3500,3250,3100,2950,2850,1620,1575 H. Res. MS m/z 362.2349 (M+H) ⁺ .

166	4-amino-5-(2-(5-chloro-2-(thiophen-3-yl)phenylmethyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine	1-(4-dimethylaminophenyl)-ethanone	** procedure of Example 173, using 3-thiophenylboronic acid	IR (KBr) 3200-3450,2950-3100,1605,1580,1550 H. Res. MS m/z 472.1363 (M+H) ⁺ .
167	4-amino-5-(pentyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine	1-(4-diethylaminophenyl)-ethanone	hexanal	IR (KBr) 3430,3320,3240-2800,1580,1560,1540,1350; mp. 211-214; MS m/z 364 (M+H) ⁺ ; H. Res. MS m/z 364.2506 (M+H) ⁺ .
168	4-amino-5-hexyl-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine	1-(4-diethylaminophenyl)-ethanone	heptanal	IR (KBr) 3440,3310,3240-2800,1580,1560,1540,1350; mp. 215-217; MS m/z 378 (M+H) ⁺ ; H. Res. MS m/z 378.2654 (M+H) ⁺ .

169	4-amino-5-(2-(3-bromophenyl)ethyl)-7-(4-diethylaminophenyl)-pyrido[2,3-d]pyrimidine	1-(4-diethylaminophenyl)-ethanone	3-(3-bromophenyl)-propionaldehyde	IR (KBr) 3640-3240,3200-2800,1580,1555,1535,1345; mp. 201-202; MS m/z 476/478 (M+H) ⁺ ; H. Res. MS m/z 476.1448 (M+H) ⁺ .
170	4-amino-5-((2-bromophenyl)methyl)-7-(4-diethylaminophenyl)-pyrido[2,3-d]pyrimidine	1-(4-diethylaminophenyl)-ethanone	2-(2-bromophenyl)-acetaldehyde	IR (KBr) 3640-3240,3240-2800,1580,1555,1540,1350; mp. 130-133; MS m/z 462/464 (M+H) ⁺ ; H. Res. MS m/z 462.1297 (M+H) ⁺ .
171	4-amino-5-cyclopropyl-7-(4-dimethylaminophenyl)-pyrido[2,3-d]pyrimidine	1-(4-dimethylaminophenyl)-ethanone	cyclopropanecarboxaldehyde	IR (KBr) 3490,3290,3240-2760,1610,1580,1540,1375; mp. 235-237; MS m/z 462/464 (M+H) ⁺ ;
172	4-amino-5-cyclohexyl-7-(4-dimethylaminophenyl)-pyrido[2,3-d]pyrimidine	1-(4-dimethylaminophenyl)-ethanone	cyclohexanecarboxaldehyde	IR (KBr) 3640-3000,2980-2760,1610,1580,1540,1345; mp. 231-234; MS m/z 462/464 (M+H) ⁺ ;

173	4-amino-5-((2-bromo-5-chlorophenyl)methyl)-7-(4-diethylaminophenyl)-pyrido[2,3-d]pyrimidine	1-(4-dimethylaminophenyl)-ethanone	2-(2-bromo-5-chlorophenyl)-acetaldehyde	IR (KBr) 3460.3220- 2760.1610,1575.15 35.1365; mp. 185- 187; MS m/z 462/464 (M+H) ⁺ ;
174	4-amino-5-methyl-7-(4-diethylaminophenyl)-pyrido[2,3-d]pyrimidine	1-(4-dimethylaminophenyl)-ethanone	acetaldehyde	IR (KBr) 3640- 3250.3250- 2760.1610,1585,15 60.1350; mp. 238- 246; MS m/z 462/464 (M+H) ⁺ ;

* prepared from the compound of Example 157 by reaction with $Pd(PPh_3)_4$ and zinc cyanide in DMF under Suzuki reaction conditions.

** prepared from the compound of Example 173 by reaction with 2-thiopheneboronic acid, $Pd(PPh_3)_4$ and aqueous sodium carbonate under Suzuki reaction conditions.

5

Examples 175-188

Following the procedures of Example 1, except substituting the appropriate reagents for the R^1 and R^3 reagents of Example 1 as indicated in Table 4 below, 10 compounds of Examples 175-188 were prepared. The treatment with aqueous HCl was omitted, and the free bases were obtained except as indicated.

Table 4
Examples 175-188

15

Ex. No.	Name	R^4 Reagent (for 7-position)	R^3 Reagent (for 5-position)	Analytical Data
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175	4-amino-5-(2,3-methylenedioxyphenyl)-7-(4-dimethylaminophenyl)-pyrido[2,3-d]pyrimidine	1-(4-dimethylaminophenyl)-ethanone	2,3-methylenedioxybenzaldehyde	IR (KBr) 3500-2500,1595,1580,1375; mp. 290-305;
176	4-amino-5-(3-fluoro-5-trifluoromethylphenyl)-7-(4-dimethylaminophenyl)-pyrido[2,3-d]pyrimidine	1-(4-dimethylaminophenyl)-ethanone	3-fluoro-5-trifluoromethylbenzaldehyde	IR (KBr) 3500,3440-3240,3200-2800,1610,1580,1560,1540,1370; mp. 293-296; MS m/z 428 (M+H) ⁺ ; H. Res. MS m/z 428,1509 (M+H) ⁺ .
177	4-amino-5-(2-bromophenyl)-7-(4-dimethylaminophenyl)-pyrido[2,3-d]pyrimidine	1-(4-dimethylaminophenyl)-ethanone	2-bromo-benzaldehyde	IR (KBr) 3480,3440-3240,3200-2800,1610,1575,1555,1535,1355; mp. 261-263; MS m/z 420/422 (M+H) ⁺ ; H. Res. MS m/z 420,0823 (M+H) ⁺ .

178	4-amino-5-(3,5-dimethylphenyl)-7-(4-dimethylaminophenyl)-pyrido[2,3-d]pyrimidine	1-(4-dimethylaminophenyl)-ethanone	3,5-dimethylbenzaldehyde	IR (KBr) 3480,3440- 3240,3200- 2800,1610,1575,15 55,1535,1360; mp. 284-286; MS m/z 370 (M+H) ⁺ ; H. Res. MS m/z 370.2036 (M+H) ⁻ .
179	4-amino-5-(3,4-dichlorophenyl)-7-(4-dimethylaminophenyl)-pyrido[2,3-d]pyrimidine	1-(4-dimethylaminophenyl)-ethanone	3,4-dichlorobenzaldehyde	IR (KBr) 3490,3440- 3240,3200- 2800,1610,1575,15 60,1535,1355; mp. 288-291; MS m/z 410/412 (M+H) ⁺ ; H. Res. MS m/z 410.0948 (M+H) ⁻ .
180	4-amino-5-(4-fluoro-3-trifluoromethylphenyl)-7-(4-dimethylaminophenyl)-pyrido[2,3-d]pyrimidine	1-(4-dimethylaminophenyl)-ethanone	4-fluoro-3-trifluoromethylbenzaldehyde	IR (KBr) 3500,3440- 3240,3200- 2800,1610,1580,15 60,1540,1505,1360; mp. 254-257; MS m/z 428 (M+H) ⁺ ; H. Res. MS m/z 428.1487 (M+H) ⁻ .

181	4-amino-5-(3-bromo-5-methoxyphenyl)-7-(4-morpholinylphenyl)-pyrido[2,3-d]pyrimidine	1-(4-morpholinylphenyl)-ethanone	3-bromo-5-methoxybenzaldehyde	IR (KBr) 3470.3440- 3240.3200- 2800.1605.1580,15 60; mp. 257-260; MS m/z 492/494 (M+H) ⁺ .
182	4-amino-5-(3-bromo-5-methoxyphenyl)-7-(4-pyrrolidinylphenyl)-pyrido[2,3-d]pyrimidine	1-(4-pyrrolidinylphenyl)-ethanone	3-bromo-5-methoxybenzaldehyde	IR (KBr) 3470.3440- 3240.3200- 2800.1610.1580,15 60,1540,1355; mp. d 250; MS m/z 476/478 (M+H) ⁺ .
183	4-amino-5-(3-bromo-5-methoxyphenyl)-7-(4-piperidinylphenyl)-pyrido[2,3-d]pyrimidine	1-(4-piperidinylphenyl)-ethanone	3-bromo-5-methoxybenzaldehyde	IR (KBr) 3470.3440- 3240.3200- 2800.1565; mp. 224-244; MS m/z 490/492 (M+H) ⁺ ;

184	4-amino-5-(3-bromo-5-methoxyphenyl)-7-(4-dimethylaminophenyl)-pyrido[2,3-d]pyrimidine	1-(4-dimethylaminophenyl)-ethanone	3-bromo-5-methoxybenzaldehyde	IR (KBr) 3470,3420- 3240,3200- 2800,1610,1575,155,1535,1355; mp. 262-266; MS m/z 450/452 (M+H) ⁺ ; H. Res. MS m/z 450.0944 (M+H) ⁺ .
185	4-amino-5-(3-methylthiophenyl)-7-(4-dimethylaminophenyl)-pyrido[2,3-d]pyrimidine	1-(4-dimethylaminophenyl)-ethanone	3-methylthio-benzaldehyde	IR (KBr) 3460,3420- 3240,3200- 2800,1605,1575,1560,1535,1355; mp. 184-220; MS m/z 388 (M+H) ⁺ ; H. Res. MS m/z 388.1586 (M+H) ⁺ .
186	4-amino-5-(3-bromo-5-methoxyphenyl)-7-(thiophene-2-yl)-pyrido[2,3-d]pyrimidine	1-(thiophene-2-yl)-ethanone	3-bromo-5-methoxybenzaldehyde	IR (KBr) 3470,3350- 2200,1700,1640,1580,1435,1365,1270; mp. 246-249; MS m/z 413/415 (M+H) ⁺ ; H. Res. MS m/z 413.0069 (M+H) ⁺ .

187	4-amino-5-(2,3-dimethoxyphenyl)-7-(4-dimethylaminophenyl)-pyrido[2,3-d]pyrimidine ***	1-(4-dimethylaminophenyl)-ethanone	2,3-dimethoxy-benzaldehyde	IR (KBr) 3480,3440- 3240,3200- 2800,1610,1580,15 50,1530,1360; mp. 222-225; MS m/z 402 (M+H) ⁺ ; H. Res. MS m/z 402.1922 (M+H) ⁺ .
188	4-amino-5-(3-methylsulfonylphenyl)-7-(4-dimethylaminophenyl)-pyrido[2,3-d]pyrimidine	1-(4-dimethylaminophenyl)-ethanone	3-methylsulfonyl-benzaldehyde	IR (KBr)3490,3400- 2800,1610,1580,15 55,1535,1355; mp. 245~270; MS m/z 420 (M+H) ⁺ ; H. Res. MS m/z 420.1493 (M+H) ⁺ .

Example 1894-acetylamino-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine

5 A suspension of 4-amino-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine (from Example 15, 0.28 g, 0.67 mole) in pyridine (3 mL) was treated with acetic anhydride (0.10 g, 1.0 mmol) and the reaction mixture was stirred for 4 hours at 25 °C. The volatiles were removed under reduced pressure, and the residue was purified by flash chromatography (SiO₂, EtOAc/hexanes) to 10 provide the title compound (0.23 g, 73% theoretical): IR (KBr) 3368, 3048, 1695, 1567; MS m/z 462/464 (M+H)⁺.

Examples 190-198

Following the procedures of Example 189, except substituting the appropriate acylating reagent for the acetic anhydride of Example 189 as indicated in Table 5 below, compounds of Examples 190-198 were prepared.

5

Table 5
Examples 190-198

Ex. No.	Name	Acyling Reagent	Analytical Data
190	4-formylamino-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)-pyrido[2,3-d]pyrimidine--190	acetic anhydride and formic acid	IR (KBr) 3382, 3047, 1704, 1570; MS m/z 448/450 (M+H) ⁺ .
191	4-(methoxyacetyl)amino-5-(3-bromophenyl)-7-(4-diethylaminophenyl)-pyrido[2,3-d]pyrimidine	methoxyacetyl chloride	IR (KBr) 3344, 3044, 1731, 1561; MS m/z 492/494 (M+H) ⁺ .
192	4-trifluoroacetylamino-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)-pyrido[2,3-d]pyrimidine	trifluoroacetic anhydride	IR (KBr) 3426, 3072, 1610, 1578; MS m/z 516/518 (M+H) ⁺ .
193	4-pentanoylamino-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)-pyrido[2,3-d]pyrimidine	pentanoyl chloride	IR (KBr) 3408, 2954, 1699, 1569; MS m/z 504/506 (M+H) ⁺ .
194	4-benzoylamino-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)-pyrido[2,3-d]pyrimidine	benzoic anhydride	IR (KBr) 3420, 3056, 1606, 1583; MS m/z 524/526 (M+H) ⁺ .

195	4-(N-BOC-glycyl)amino-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)-pyrido[2,3-d]pyrimidine	N-BOC-glycyl-imidazole	IR (KBr) 3362, 2975, 1719, 1570; MS m/z 577/579 (M+H) ⁺ .
196	4-(N-phthalimidylglycyl)amino-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)-pyrido[2,3-d]pyrimidine	N-phthalimidyl-glycyl-chloride	IR (KBr) 3408, 2927, 1719, 1570; MS m/z 607/609 (M+H) ⁺ .
197	4-(ethoxycarbonyl)amino-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)-pyrido[2,3-d]pyrimidine	diethyl dicarbonate	IR (KBr) 3405, 2987, 1738, 1569; MS m/z 492/494 (M+H) ⁺ .
198	4-(ethylaminocarbonyl)amino-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)-pyrido[2,3-d]pyrimidine	ethyl isocyanate	IR (KBr) 3405, 3053, 1701, 1548; MS m/z 491/493 (M+H) ⁺ .

Example 199

4-allylamino-5-(4-bromophenyl)-7-(4-dimethylaminophenyl) pyrido [2,3-d] pyrimidine

5 The product was prepared by treating a solution of 4-chloro-5-(p-dimethylaminophenyl)-7-(p-bromophenyl)pyrido[2,3-d]pyrimidine in CH_2Cl_2 -TEA with allylamine and heating the resulting mixture at reflux for 1 hour. The volatiles were removed under reduced pressure, and the residue was purified by flash chromatography (SiO_2 , EtOAc/hexanes) to provide the title compound IR (KBr) 3437, 1564, 1355, 1195;

10 MS m/z 460/462 (M+H)⁺.

The 4-chloro-5-(p-dimethylaminophenyl)-7-(p-bromophenyl)pyrido [2,3-d]pyrimidine was prepared as follows.

A sample of 4-(4-bromophenyl)-3-cyano-6-(4-(dimethylamino)phenyl)pyridine-2-amine (from Example 1, 5.0 g, 12.7 mmol) in 20 mL of H_2SO_4 was heated at 80 °C for 30

minutes. Ice was added, and the reaction mixture was neutralized with aqueous NaOH. The resulting crude 3-carboxamide was collected by filtration, triturated with EtOAc-hexanes, then dried under reduced pressure (4.95 g, 95% theoretical). A solution of the carboxamide (4.25 g, 10.3 mmol) in triethylorthoformate (20 mL) was treated with p-toluenesulfonic acid (catalytic) and the reaction mixture was warmed at 80 °C for 4 hours. The volatiles were removed and the crude bicyclic 4-hydroxyl-5-(p-dimethylaminophenyl)-7-(p-bromophenyl)pyrido[2,3-d]pyrimidine product was suspended in POCl₃ (15 mL) then warmed at 100 °C for 2 hours. The POCl₃ was removed under reduced pressure to provide crude 4-chloro-5-(p-dimethylaminophenyl)-7-(p-bromophenyl)pyrido[2,3-d]pyrimidine. The invention therefore relates to intermediate compounds of formula III wherein X is selected from hydroxyl or halogen and the remaining variables are the same as in formula I or II.

Example 200

15 4-(2-(N,N-dimethylamino)ethylamino)-5-(4-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine trihydrochloride

The product was prepared by treating a solution of 4-chloro-5-(p-dimethylaminophenyl)-7-(p-bromophenyl)pyrido[2,3-d]pyrimidine (prepared as in Example 199) in CH₂Cl₂-TEA with the 2-(dimethylamino)ethylamine and heating the resulting mixture at reflux for 1 hour. The volatiles were removed under reduced pressure, and the residue was purified by flash chromatography (SiO₂, EtOAc/hexanes) to provide the title compound. The product was treated with excess 2M HCl (aq) followed by lyophilization to give the product as the trihydrochloride salt; IR (KBr) 3385, 1561, 1356, 1197; MS m/z 491/493 (M+H)⁺.

25

Example 201

30 4-(4-(N,N-dimethylamino)butylamino)-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine tetrahydrochloride

The product was prepared by treating a solution of 4-amino-5-(p-dimethylaminophenyl)-7-(p-bromophenyl)pyrido[2,3-d]pyrimidine in CH₂Cl₂-TEA

with the 4-(dimethylamino)butylamine and heating the resulting mixture at reflux for 1 hour. The volatiles were removed under reduced pressure, and the residue was purified by flash chromatography (SiO₂, EtOAc/hexanes). The product was treated with excess 2M HCl (aq) followed by lyophilization to give the product as the 5 tetrahydrochloride salt; IR (KBr) 3439, 1567, 1356, 1196; MS m/z 519/521 (M+H)⁺.

Example 202

4-(N-allyl-N-formylamino)-5-(4-dimethylaminophenyl)-7-

(p-bromophenyl)pyrido[2,3-d]pyrimidine

10 A sample of the compound from Example 190 above, 4-formylamino-5-(2-phenylethyl)-7-(4-diethylaminophenyl)-pyrido[2,3-d]pyrimidine (0.27 g, 0.6 mmol) in 3 mL of a 4:1 mixture of THF and DMF at 0°C was treated with NaH (60% dispersion, 36 mg, 0.9 mmol) and the solution was stirred for 0.5 hour. Allyl 15 bromide (0.29 g, 2.4 mmol) was added, and the reaction mixture was stirred for an additional 0.5 hour. Aqueous workup followed by flash chromatography provided the title compound: LRMS m/z 488/490. IR (cm⁻¹) 3428, 2910, 1696, 1551, 1362, 1193.

Example 203

4-diacetylamino-5-(4-dimethylaminophenyl)-7-(p-bromophenyl)-
pyrido[2,3-d]pyrimidine

This compound was isolated as a minor product from the reaction mixture of Example 190 above: LRMS m/z 504/506. IR (cm⁻¹) 2922, 1726, 1550, 1360, 1197.

25

Example 204

4-amino-5-(3-bromophenyl)-7-(5-amino-2-pyridyl)pyrido[2,3-d]pyrimidine

30 A solution of 5-aminopyridine-2-ethanone (1.15 g, 8.45 mmol), 3-bromobenzaldehyde (1.70 g, 9.2 mmol), malononitrile (0.61 g, 9.2 mmol), and

ammonium acetate (1.15 g, 15 mmol) in 25 mL of benzene was heated at reflux with azeotropic removal of water. After 6 hours the reaction mixture was concentrated, and the desired intermediate (1.82 g, 49%) was isolated following flash chromatography (SiO₂, EtOAc-CH₂Cl₂). LRMS m/z 366/368. The intermediate was suspended in 15 mL of formamide, and the reaction mixture was heated at 180 °C for 4 hours. The solution was cooled to 25 °C, 10 mL of 4M HCl (aq) was added, and the mixture was stirred for 1 hour. The aqueous solution was neutralized with NaOH (aq), and the precipitate was collected by filtration. The title compound (1.3 g, 68%) was isolated following flash chromatography of the precipitate: LRMS m/z 393/395;

10 IR (cm⁻¹) 3481, 3161, 1620, 1573, 1483, 1359.

The 5-aminopyridine-2-carboxaldehyde starting material was prepared as follows:

204a. 5-amino-2-bromopyridine

A solution of 2-bromo-5-nitropyridine (5.1 g, 25 mmol) in 50 mL of a 10:1 mixture of acetic acid and water was treated with iron powder (7.8 g, 140 mmol) in several portions over 20 minutes. After an additional 30 minutes the volatiles were removed under reduced pressure, and the residue was quenched with 5% aqueous sodium carbonate. The aqueous solution was extracted with methylene chloride, and the combined organic layer was dried (sodium sulfate) then concentrated in vacuo to provide the desired product 20 as a white solid (4.25 g, 98%).

204b. 5-aminopyridine-2-ethanone

A sample of 5-amino-2-bromopyridine (4.25 g, 24 mmol), PdCl₂(PPh₃)₂ (0.34 g, 2 mol%), CuI (0.09 g, 2 mole%), and trimethylsilylacetylene (3.0 g, 31 mmol) were dissolved in 100 mL of a 4:1 mixture of triethylamine and acetonitrile, and the reaction mixture was stirred 24 hours at 25 °C. The reaction mixture was concentrated, and the residue was dissolved in 100 mL of a 10:1 mixture of acetone and water. Hg(O₂CCF₃)₂ (11.1 g, 26 mmol) and H₂SO₄ (72 mmol) were added to the reaction mixture, and the solution was heated at reflux for 2 hours. The reaction mixture was cooled to 25 °C and 30 neutralized with saturated aqueous sodium carbonate. The aqueous layer was extracted

with methylene chloride, then the combined organic layer was dried (Na_2SO_4) and concentrated in vacuo. Flash chromatography (SiO_2 , EtOAc-Hexanes) provided the title compound: LRMS m/z 137 ($M = \text{H}^+$); IR (cm^{-1}) 3428, 1668, 1646, 1582, 1358, 1274.

5

Example 2054-amino-5-(3-bromophenyl)-7-(5-dimethylamino-2-pyridyl)pyrido[2,3-d]pyrimidine trihydrochloride salt

Following the procedure of Example 204, 5-dimethylaminopyridine-2-ethanone was reacted with bromobenzaldehyde, malononitrile, and ammonium acetate to give the title compound. The residue was triturated with excess HCl/ether, the volatiles were removed under reduced pressure, and the title compound was dried under high vacuum: LRMS m/z 421/423. IR (cm^{-1}) 3245, 1664, 1545, 1395.

The 5-dimethylaminopyridine-2-carboxaldehyde starting material was prepared as follows:

205a. 3-N,N-dimethylaminopyridine

A solution of 3-aminopyridine (9.4 g, 0.10 mol) in a 1:1 mixture of formic acid (96%) and formaldehyde (37% aqueous solution) was heated at reflux for 18 hours. The volatiles were removed under reduced pressure and the residue was neutralized with saturated aqueous NaHCO_3 . The aqueous layer was extracted with CH_2Cl_2 , then the combined organic layer was dried (Na_2SO_4) and concentrated under reduced pressure. Flash chromatography (SiO_2 , EtOAc-Hexanes) provided the title compound: (11.1 g, 91%), LRMS m/z 123 ($M + \text{H}^+$).

25

205b. 2-bromo-5-N,N-dimethylaminopyridine

A solution of 3-N,N-dimethylaminopyridine (5.88 g, 48.1 mmol) in 150 mL of CH_2Cl_2 at 0 °C was treated with 2,4,4,6-tetrabromo-2,5-cyclohexadienone (20.7 g, 50 mmol) in several portions over 30 minutes. After 2 hours at 0 °C the reaction

mixture was concentrated, and the desired 2-bromo-5-N,N-dimethylaminopyridine was isolated following flash chromatography (16.5 g., 82%): LRMS m/z 201/203.

204c. 5-N,N-dimethylaminopyridine-2-ethanone

5 Following the procedure of Example 203b, 2-bromo-5-N,N-dimethylaminopyridine, except converting the compound to the trihydrochloride salt by treatment with HCl/ether, was converted to the title compound: LRMS m/z 165; IR (cm⁻¹) 3480, 1666, 1581, 1368, 1272.

10 Example 206

4-amino-5-(3-bromophenyl)-7-(5-dimethylamino-2-pyrazinyl)-pyrido[2,3-d]pyrimidine hydrochloride

15 Following the procedure of Example 204, 5-dimethylaminopyrazine-2-ethanone was reacted with bromobenzaldehyde, malononitrile, and ammonium acetate to give the title compound. The residue was triturated with excess HCl/ether, the volatiles were removed under reduced pressure, and the title compound was dried under high vacuum: LRMS m/z 422/424. IR (cm⁻¹) 3310, 1630, 1525, 1444, 1375.

20 The 5-dimethylaminopyrazine-2-carboxaldehyde starting material was prepared as follows:

206a. 5-dimethylaminopyrazine-2-ethanone

25 A solution of 5-hydroxypyrazine-2-carboxylic acid (4.0 g, 28.5 mmol) in 50 mL of thionyl chloride and 0.1 mL of DMF was heated at reflux for 8 hours. The volatiles were removed under reduced pressure, and the residue was dissolved in 20 mL of toluene. This solution was added to a solution of dimethyl malonate (4.75 g, 36 mmol), MgCl₂ (2.09 g, 22 mmol) and triethyl amine (7.08 g, 70 mmol) in 100 mL of toluene. The reaction mixture was stirred for 1 hour at 25 °C, quenched by addition of water, and the product was extracted with methylene chloride. The 30 solvent was removed, the crude intermediate was dissolved in 25 mL of a 25:1

mixture of DMSO and water, and the resulting solution was warmed at 150 °C for 2 hours. The reaction was quenched by addition of water, and the product was extracted with methylene chloride to provide 2-acetyl-5-chloropyrazine (LRMS m/z 156). This intermediate was treated with aqueous dimethylamine at room 5 temperature for 30 minutes to afford 5-dimethylaminopyrazine-2-ethanone (LRMS m/z 166); LRMS m/z 422/424; IR (cm⁻¹) 3310, 1630, 1525, 1444, 1375.

Example 207

4-amino-5-(3-bromophenyl)-7-(2-oxobenzoxazolin-6-yl)pyrido[2,3-d]pyrimidine

10

Following the procedure of Example 204, 2-oxobenzoxazolin-6-ethanone was reacted with bromobenzaldehyde, malononitrile, and ammonium acetate to prepare the title compound: LRMS m/z 434/436; IR (cm⁻¹) 3095, 1760, 1579, 1481, 1350.

15

The 2-oxobenzoxazolin-5-ethanone starting material was prepared as follows:

207a. 2-oxobenzoxazolin-6-ethanone

DMF (9 mL) was added dropwise to AlCl₃ (58.7 g, 440 mmol) over 20 minutes and the resulting suspension was stirred 15 minutes at 25 °C. Acetic 20 anhydride (7.14 g, 70 mmol) and 2-benzoxazolinone (6.0 g, 44 mmol) were added and the reaction mixture was warmed at 80 °C and stirred for 4 hours. The mixture was cooled to 25 °C and poured into ice/H₂O. The resulting precipitate was collected by filtration and dried under vacuum to provide the title compound (6.4 g, 81%, LRMS m/z 177).

25

Example 208

4-amino-5-(3-bromophenyl)-7-(1-methyl-2-oxobenzoxazolin-6-yl)-pyrido[2,3-d]pyrimidine

Following the procedure of Example 204, 1-methyl-2-oxobenzoxazolin-5-ethanone was reacted with bromobenzaldehyde, malononitrile, and ammonium acetate to prepare the title compound: LRMS m/z 448/450; IR (cm⁻¹) 3440, 1782, 1605, 1458, 1350.

5 The 1-methyl-2-oxobenzoxazolin-5-ethanone starting material was prepared as follows:

208a. 1-methyl-2-oxobenzoxazolin-5-ethanone

A solution of 2-oxobenzoxazolin-5-ethanone (from Example 206a, 2.50 g, 10 14.1 mmol) in 20 mL of a 4:1 mixture of THF and DMF at 0 °C was treated with NaH (60 % dispersion, 0.8 g, 20 mmol) and the mixture was stirred 20 minutes at 0 °C. Methyl iodide (3.97 g, 28 mmol) was added and the reaction mixture was warmed to 25 °C and stirred for 15 minutes. Saturated aqueous NaHCO₃ was added and the aqueous layer was extracted with CH₂Cl₂. The desired product (2.55 g, 94%, 15 LRMS m/z 191), was isolated following flash chromatography (SiO₂, EtOAc-CH₂Cl₂).

Example 209

4-amino-5-((5-chloro-2-(3-methoxyphenyl)phenyl)methyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine

20 The title compound was prepared from the compound of Example 173 by reaction with 3-methoxyphenylboronic acid, Pd(PPh₃)₄ and aqueous sodium carbonate under Suzuki reaction conditions. IR (KBr) 3550-3250, 3240-2760, 1580, 1560, 1540, 1350; H. Res. MS m/z 496.1902 (M+H)⁺.

25

Example 210

4-amino-5-((2-bromophenyl)methyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine

Following the procedures of Example 157, except substituting 1-(4-dimethylaminophenyl)-ethanone for the R¹ reagent and 2-(2-bromophenyl)-

acetaldehyde for the R¹ reagent of Example 157, the title compound was prepared as shown in Table 6.

Table 6

Ex. No.	Name	R ⁴ Reagent (for 7-position)	R ⁵ Reagent (for 5-position)	Analytical Data
210	4-amino-5-((2-bromophenyl)methyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine	1-(4-dimethylaminophenyl)-ethanone	2-(2-bromophenyl)-acetaldehyde	IR (KBr); MS m/z 434,436 (M+H) ⁺ .

5

Example 211

4-amino-5-(2-((thiophene-2-yl)phenyl)methyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine

The title compound was prepared from the compound of Example 173 by reaction with 2-thiopheneboronic acid, Pd(PPh₃)₄, and aqueous sodium carbonate 10 under Suzuki reaction conditions. IR (KBr) 3640-3240, 3240-2800, 1580, 1560, 1540, 1350; H. Res. MS m/z 466.2070 (M+H)⁺.

Example 212

4-amino-5-(2-((thiophene-3-yl)phenyl)methyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine

The title compound was prepared from the compound of Example 173 by reaction with 3-thiopheneboronic acid, Pd(PPh₃)₄, and aqueous sodium carbonate under Suzuki reaction conditions. IR (KBr) 3640-3240, 3240-2800, 1580, 1560, 1540, 1350; H. Res. MS m/z 466.2057 (M+H)⁺.

15
20

Examples 213-222

Following the procedures of Example 1, except substituting the appropriate reagents for R⁴ and R³ as indicated in Table 7 below, compounds of Examples 212-222 were prepared.

5

Table 7
Examples 213-222

Ex. No.	Name	R ⁴ Reagent (for 7-position)	R ³ Reagent (for 5-position)	Analytical Data
213	4-amino-5-(3-bromophenyl)-7-(4-(N-formyl-N-(2-methoxyethyl)amino)phenyl)pyrido[2,3-d]pyrimidine;	1-(4-(N-formyl-N-(2-methoxyethyl)amino)phenyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3490, 1689, 1120, 800 cm ⁻¹ ; MS m/z 478/480 (M+H) ⁺ .
214	4-amino-5-(3-bromophenyl)-7-(4-(N-(2-methoxyethyl)amino)phenyl)pyrido[2,3-d]pyrimidine;	* 1-(4-(N-2-methoxyethyl)amino)phenyl-ethanone	3-bromo-benzaldehyde	IR (KBr) 3330, 2925, 1675, 800 cm ⁻¹ ; MS m/z 451/453 (M+H) ⁺ .
215	4-amino-5-(3-bromophenyl)-7-(4-(N-methyl-N-(2-dimethylamino)ethyl)amino)phenyl)pyrido[2,3-d]pyrimidine;	1-(4-(N-methyl-N-(2-dimethylamino)ethyl)amino)phenyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3440, 1600, 1160, 810 cm ⁻¹ ; MS m/z 477/479 (M+H) ⁺ .

216	4-amino-5-(3-bromophenyl)-7-(4-(2-methoxyacetylamo)ethyl)amino)phenyl)pyrido[2,3-d]pyrimidine;	** 1-(4-(2-methoxyacetylamo)ethyl)amino)phenyl-ethanone	3-bromo-benzaldehyde	IR (KBr) 3480, 1520, 710 cm ⁻¹ ; MS m/z 464,466 (M+H) ⁺ .
217	4-amino-5-(3-bromophenyl)-7-((4-formylamino)phenyl)pyrido[2,3-d]pyrimidine;	***1-(4-(formylamino)phenyl-ethanone	3-bromo-benzaldehyde	IR (KBr) 3475, 1690, 1355, 800 cm ⁻¹ ; MS m/z 420/422 (M+H) ⁺ .
218	4-amino-5-(3-bromophenyl)-7-(4-(2-(dimethylamino)acetyl)amino)phenyl)pyrido[2,3-d]pyrimidine;	****1-(4-(2-dimethylamino)acetyl)amino)phenyl-ethanone	3-bromo-benzaldehyde	IR (KBr) 3452, 1605, 1250, 590 cm ⁻¹ ; MS m/z 477/479 (M+H) ⁺ .
219	4-amino-5-(3-bromophenyl)-7-(4-(2-oxo-3-oxazolidinyl)phenyl)pyrido[2,3-d]pyrimidine;	1-(4-(2-oxo-3-oxazolidinyl)phenyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3480, 1750, 1400, 700 cm ⁻¹ ; MS m/z 462/464 (M+H) ⁺ .
220	4-amino-5-(3-bromophenyl)-7-(6-(2-propyl)-3-pyridinyl)pyrido[2,3-d]pyrimidine trihydrochloride	1-(6-(2-propyl)-3-pyridinyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3474, 3098, 1636, 1566, 1499, 1352, 1282 cm ⁻¹ ; MS m/z 393 (M+H) ⁺ .

221	4-amino-5-(3-bromophenyl)-7-(3-methyl-4-pyrrolidinylphenyl)pyrido[2,3-d]pyrimidine dihydrochloride	1-(3-methyl-4-pyrrolidinylphenyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3440, 1640, 1607, 1586, 1370 cm ⁻¹ ; MS m/z 433 (M+H) ⁺ .
222	4-amino-5-(3-bromophenyl)-7-(6-imidazolyl-3-pyridinyl)pyrido[2,3-d]pyrimidine trihydrochloride	1-(6-imidazolyl-3-pyridinyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3028, 1641, 1607, 1595, 1375cm ⁻¹ ; MS m/z 417 (M+H) ⁺ .

*prepared by deformylation of Example 213 with dilute HCl in methanol.

**prepared by acylation of Example 213 with 2-methoxyacetyl chloride/pyridine.

***prepared by formylation of the 7-(3-bromophenyl)-2-cyano-5-(4-aminophenyl)pyridine-2-amine intermediate.

5 ****prepared by acylation of Example 213 with the 2-(dimethylamino)acetyl chloride.

Examples 223-225

Following the procedures of Example 157, except substituting the appropriate 10 reagents for the R⁴ and R³ reagents of Example 157 as indicated in Table 8 below, compounds of Examples 223-225 were prepared.

Table 8

Examples 223-225

15

Ex. No.	Name	R ⁴ Reagent (for 7-position)	R ³ Reagent (for 5-position)	Analytical Data
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223	4-amino-5-phenylmethyl-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine	1-(4-diethylaminophenyl)-ethanone	2-phenyl-acetaldehyde	IR (KBr) 3450,3380,2850-3200,1605,1580,1560,1540; H. Res. MS m/z 384,2176 (M+H) ⁺ .
224	4-amino-5-(2-(3-aminopropynyl)phenylmethyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine	1-(4-diethylaminophenyl)-ethanone	* from Example 170, palladium coupling with 3-aminopropyne	IR (KBr) 2400-170, palladium coupling with 3-aminopropyne 3450,2050,2120,1650,1605,1540; MS m/z 437 (M+H) ⁺ .
225	4-amino-5-(1-(2-bromophenyl)ethyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine	1-(4-dimethylaminophenyl)-ethanone	2-(2-bromophenyl)-propionaldehyde	IR (KBr) 3520,3250-3500,2850-3150,1605,1580,1560,1540; H. Res. MS m/z 448,1137 (M+H) ⁺ .

*prepared from the compound of Example 170 by reaction with propargylamine, CuI and Pd(PPh₃)₄ under Suzuki reaction conditions.

Examples 226-228

5 Following the procedures of Example 1, except substituting the appropriate reagents for R⁴ and R³ as indicated in Table 9 below, compounds of Examples 226-228 were prepared.

Table 9
Examples 226-228 .

Ex. No.	Name	R ¹ Reagent (for 7- position)	R ³ Reagent (for 5- position)	Analytical Data
226	4-amino-5-(4-dimethylaminophenyl)-7-(4-bromophenyl)pyrido[2,3-d]pyrimidine	1-(4-bromophenyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3456, 3053, 16600, 1556 cm ⁻¹ ; MS m/z 420 (M+H) ⁺ .
227	4-amino-5-(2-furanyl)-7-(4-(N-morpholinyl)phenyl)pyrido[2,3-d]pyrimidine	1-(4-(N-morpholinyl)phenyl)ethanone	furan-2-carboxaldehyde	IR (KBr) 3460, 1600, 1580, 1457 cm ⁻¹ ; MS m/z 374 (M+H) ⁺ .
228	4-amino-5-(3-bromophenyl)-7-(2-dimethylamino-5-pyrimidinyl)pyrido[2,3-d]pyrimidine	1-(5-(2-(dimethylamino)pyrimidinyl)ethane	3-bromo-benzaldehyde	IR (KBr) 3442, 1640, 1604, 1577, 1536, 1408, 1367, 1348 cm ⁻¹ ; MS m/z 422 (M+H) ⁺ .

5

Example 229

4-amino-5-(3-bromophenyl)-7-(4-(ureido)phenyl)pyrido[2,3-d]pyrimidine

A solution of 4-amino-5-(3-bromophenyl)-7-(4-aminophenyl)pyrido[2,3-d]pyrimidine (Example 71, 310 mg, 0.79 mmol) in 2 mL of acetic acid was treated with 10 sodium cyanate (56 mg, 0.87 mmol), and the reaction mixture was stirred for 30 minutes at 25 °C. The solution was concentrated and the residue was suspended in aqueous

NaHCO₃. The crude product was collected by filtration, then purified by flash chromatography. The product was dissolved in methanol and treated with excess 2M aqueous HCl to provide the hydrochloride salt: LRMS m/z 435/437. IR (cm⁻¹) 3442, 2212, 3186, 3059, 1681, 1582, 1525, 1358.

5

Example 230

4-amino-5-(1-phenylmethyl-3-piperidinyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine

10 Following the procedures of Example 157, except substituting 1-(4-diethylamino-phenyl)-ethanone for the R⁴ reagent and 1-phenylmethylpiperidine-3-carboxaldehyde (prepared as described by Gilligan et al., J. Med. Chem., 35:4344-4361 (1992)) for the R³ reagent thereof, the title compound was prepared. The treatment with aqueous HCl was omitted, and the free base was obtained. IR (KBr) 3440, 3100-2800-1640, 1605, 1595, 1535 cm⁻¹; MS m/z 467 (M+H)⁺; mp 218-220 °C.

Examples 231-243

Following the procedures of Example 1, except substituting the appropriate reagents for R⁴ and R³ as indicated in Table 10 below, compounds of Examples 230-243 20 were prepared. In some cases, the treatment with aqueous HCl was omitted, and the free bases were obtained. Some compounds were isolated as the TFA salt following purification via high pressure liquid chromatography (HPLC).

Table 10
Examples 231-243

Ex. No.	Name	R ¹ Reagent (for 7-position)	R ³ Reagent (for 5-position)	Analytical Data
231	4-amino-5-(3-bromophenyl)-7-(6-(3-methyl-5-isoxazolyl))-3-pyridinyl)pyrido[2,3-d]pyrimidine;	1-(6-(3-methyl-5-isoxazolyl))-3-pyridinyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3484, 1635, 1574, 1562, 1352 cm ⁻¹ ; MS m/z 459 (M+H) ⁺ .
232	4-amino-5-(3-bromophenyl)-7-(6-chloro-3-pyridinyl)pyrido[2,3-d]pyrimidine;	1-(6-chloro-3-pyridinyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3478, 1608, 1574, 1542 cm ⁻¹ ; MS m/z 414 (M+H) ⁺ .
233	4-amino-5-(3-bromophenyl)-7-(6-methoxy-3-pyridinyl)pyrido[2,3-d]pyrimidine;	1-(6-methoxy-3-pyridinyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3484, 1635, 1560, 1348 cm ⁻¹ ; MS m/z 409 (M+H) ⁺ .
234	4-amino-5-(3-bromophenyl)-7-(6-(1,2,4-triazol-4-yl)-3-pyridinyl)pyrido[2,3-d]pyrimidine;	1-(6-(1,2,4-triazol-4-yl))-3-pyridinyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3494, 1612, 1579, 1467, 1359, 1271, 1233 cm ⁻¹ ; MS m/z 445 (M+H) ⁺ .

235	4-amino-5-(3-bromophenyl)-7-(2-morpholinyl-5-pyrimidinyl)pyrido[2,3-d]pyrimidine;	1-(2-morpholinyl-5-pyrimidinyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3434, 1637, 1608, 1585, 1335, cm ⁻¹ ; MS m/z 463 (M+H) ⁺ .
236	4-amino-5-(2-thiazolyl)-7-(4-pyrrolidinylphenyl)-pyrido[2,3-d]pyrimidine;	1-(4-pyrrolidinylphenyl)-ethanone	2-thiazole-carboxaldehyde	IR (KBr) 3400, 1637, 1608, 1532, cm ⁻¹ ; MS m/z 376 (M+H) ⁺ .
237	4-amino-5-(3-bromophenyl)-7-(6-pyrazolyl-3-pyridinyl)-pyrido[2,3-d]pyrimidine;	1-(6-pyrazolyl-3-pyridinyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3474, 1580, 1562, 1492, 1395, cm ⁻¹ ; MS m/z 444 (M+H) ⁺ .
238	4-amino-5-(3-bromophenyl)-7-(4-(1-methyl-ureido)phenyl)-pyrido[2,3-d]pyrimidine;	1-(4-(1-methyl-ureido)phenyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3400, 1665, 1350 cm ⁻¹ ; MS m/z 450 (M+H) ⁺
239	4-amino-5-(3-bromophenyl)-7-(4-(N-methyl-N-(2-pyrimidinyl)amino)phenyl)-pyrido[2,3-d]pyrimidine;	1-(4-(N-methyl-N-(2-pyrimidinyl)amino)phenyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3475, 1578, 1553, 1482, 1396, cm ⁻¹ ; MS m/z 484 (M+H) ⁺ .

240	4-amino-5-(3-bromophenyl)-7-(3-fluoro-4-(N-formyl-N-methylamino)phenyl)-pyrido[2,3-d]pyrimidine; *	1-(3-fluoro-4-(N-methylamino)phenyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3448, 1600, 1525, 1476, cm ⁻¹ ; MS m/z 484 (M+H) ⁺ .
241	4-formylamino-5-(3-bromophenyl)-7-(3-fluoro-4-(N-formyl-N-methylamino)phenyl)-pyrido[2,3-d]pyrimidine; *	1-(3-fluoro-4-(N-methylamino)phenyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3465, 1607, 1546, 1350, cm ⁻¹ ; MS m/z 481 (M+H) ⁺ .
242	4-amino-5-(3-bromophenyl)-7-(4-(N-methyl-N-methylsulfonylamino)phenyl)pyrido[2,3-d]pyrimidine;	1-(4-(N-methyl-N-methylsulfonylamino)phenyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3470, 1650, 1570, 1338, cm ⁻¹ ; MS m/z 484 (M+H) ⁺ .
243	4-amino-5-(3-bromophenyl)-7-(6-(N-methyl-N-methylsulfonylamino)-3-pyridinyl)pyrido[2,3-d]pyrimidine;	1-(6-(N-methyl-N-methylsulfonylamino)-3-pyridinyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3460, 1680, 1580, 1330 cm ⁻¹ ; MS m/z 485 (M+H) ⁺ .

* separated by chromatography from the same reaction mixture; formylation occurs during the cyclization step

Example 2444-amino-5-(3-bromophenyl)-7-(1-methyl-5-indoliny)pyrido[2,3-d]pyrimidine dihydrochloride

5 A sample of 4-(3-bromophenyl)-3-cyano-6-(1-methyl-5-indoliny)pyridine-2-amine was heated at reflux in formamide. The reaction was monitored by TLC, and when the reaction was complete the mixture was cooled to room temperature. The product was allowed to precipitate, then recovered by filtration and washed with water. Additional product was extracted from the filtrate. The product was purified
10 by column chromatography eluting with 10% MeOH/CH₂Cl₂ and converted to the hydrochloride salt by treatment with ether/HCl. The salt was isolated and dried under vacuum to give the title compound. LRMS m/z 432/434; IR (cm⁻¹) 3500, 3400, 3300, 3200-2800, 1610, 1580, 1560, 1540.

15 The 4-(3-bromophenyl)-3-cyano-6-(1-methyl-5-indolyl)pyridine-2-amine starting material was prepared as follows:

244a. 5-bromo-1-methylindoline

20 Acetic acid (60 mL) was added to a mixture of 5-bromo-1-methylindole (10 g, 47.6 mmol) and sodium cyanoborohydride (8 g). After one hour at 15 °C, the reaction was basified with aqueous NaOH and extracted with toluene. The organic phase was dried over MgSO₄ and concentrated to a powder under vacuum. This material was purified by flash chromatography to give the title compound, 8.62 g (82 %); MS 212, 214 [M+H]⁺.

244b. 5-acetyl-1-methylindoline

25 A mixture of 5-bromo-1-methylindoline (8.6 g, 40.7 mmol), trimethylsilylacetylene (12 mL), palladium bis-triphenylphosphine dichloride (600 mg), CuI (620 mg) and triethylamine (16 mL) in acetonitrile (20 mL) was heated at 75 °C for 3 days, then cooled and concentrated in vacuo. The residue was dissolved
30 in 120 mL of 1:1 ethyl acetate/hexane, and the solids were removed by filtration.

The solvent was removed and a sample of the residue (5 g) was dissolved in 90% aqueous acetone (44 mL). To this solution was added sulfuric acid (2.2 g), and Hg(OCOCF₃)₂ (9 g). The reaction was heated at reflux for 20 minutes, cooled, made basic with aqueous sodium hydroxide and extracted with ethyl acetate. The organic 5 layer was dried over MgSO₄ and concentrated to an oil, which was purified by flash chromatography to give 850 mg of the title compound: MS 176 [M+H]⁺.

244c. 4-(3-bromophenyl)-3-cyano-6-(1-methyl-5-indolinvl)pyridine-2-amine

Prepared by condensation of 1',1'-dicyano-3-bromostyrene (prepared by 10 condensation of 3-bromobenzaldehyde with malononitrile in ethanol in the presence of a catalytic amount of glycine) and the 5-acetyl-1-methylindoline (the R⁴ reagent) with ammonium acetate in ethanol. After 3.5 hours, the mixture was cooled, and the solvent was removed. The residue was purified by flash chromatography, eluting with methylene chloride, to give the title compound (588 mg, 30% yield; MS m/z 15 394 (M+H)⁺.

Example 245

4-amino-5-(3-bromophenyl)-7-(1-methyl-5-benzimidazolyl)pyrido[2,3-d]pyrimidine

20 tetrahydrochloride

The title compound was prepared according to the procedure of Example 1, except substituting 1-methyl-5-acetyl-benzimidazole (prepared according to the procedure of D. J. Evans et. al., J. Chem. Soc. Perkin Trans. II, 1978, 865) for the 4-dimethylaminobenzaldehyde (the R³ reagent) therein. IR (KBr) 3650-3230, 3230-2000, 25 1635, 1605, 1590, 1555, 1365 cm⁻¹; MS m/z 431/433, 431.0605 (M+H)⁺.

Example 246

4-amino-5-(3-bromophenyl)-7-(6-dimethylamino-3-pyridazinyl)pyrido[2,3-d]pyrimidine

30 tetrahydrochloride

246a. 6-(1-butoxyethenyl)-3-chloropyridazine

To a solution of 20 g (200 mmol) of butyl vinyl ether in 80 mL of THF at -78 °C was added 130 mL of a 1.7 M solution of t-butyl lithium in pentane over about 20 minutes. The yellow suspension was stirred while allowing to warm to 0 °C. THF (150 mL) was added, and the mixture cooled to -78 °C and a solution of 23 mL (200 mmol) of trimethyl borate in 50 mL of THF was added. The reaction was warmed to 20 °C, 20 mL of methanol was added, and the solution concentrated in vacuo. The residue was diluted with 400 mL of dioxane, and 20.9 g (140 mmol) of 3,6-dichloropyridazine, 2.31 g of Pd(PPh₃)₄, and 200 mL of 2 M aqueous sodium carbonate was added. The reaction was heated to reflux over one hour, then cooled and filtered to remove solids. The filtrate was concentrated in vacuo and partitioned between ethyl acetate and 1 M sodium hydroxide. The organic phase was dried over Na₂SO₄, concentrated in vacuo, and purified by flash chromatography to give 6.3 g (21%) of the title compound. MS {M + }+ 213, 215.

15

246b. 1-(6-chloropyridazin-3-yl)ethanone

A mixture 6.3 g of the compound from Step 246a in 40 mL of dimethoxyethane, 10 mL of water, and 4 mL of 12 M HCl was stirred for 20 minutes, then 125 mL of water was added, and the reaction was neutralized with 12 g of NaHCO₃. The reaction was extracted with ethyl acetate, dried over Na₂SO₄, and concentrated in vacuo to give a yellow solid. 4.7 g.

246c. 1-(3-(6-(dimethylamino)pyridazin-3-yl))ethanone (the R⁴ reagent)

A solution of 1.57 g (10 mmol) of 1-(6-chloropyridazin-3-yl)ethanone (from Step 25 246b) in 15 mL of dimethoxyethane was treated with 50 mmol of 40% aqueous dimethylamine. After one hour, the reaction was partitioned between CH₂Cl₂ and water. The organic phase was dried over CH₂Cl₂, and concentrated in vacuo to give the title compound.

246d. 3-acetyl-6-(dimethylamino)pyridazine

The title compound was prepared by condensing 1,1-dicyano-(3-(3-bromophenyl)propene (the R³ reagent) with the compound from Step 246c (the R⁴ reagent) and ammonium acetate in ethanol according to the procedure of Example 157d.

5

246e. 4-amino-5-(3-bromophenyl)-7-(6-dimethylamino-3-pyridazinyl)pyrido[2,3-d]pyrimidine tetrahydrochloride

The title compound was prepared from the compound of Step 246d according to the procedure of Example 157, except substituting formamide for the ammonium sulfate
10 and triethyl orthoformate thereof.

Examples 247-248

Following the procedures of Example 246, except in step (c) substituting the appropriate reagents for methylamine as indicated in the Table 11A below, compounds of
15 Examples 247-248 were prepared.

Table 11A
Examples 247-248

Ex. No.	Name	reagent of step c	Analytical Data
247	4-amino-5-(3bromophenyl)-7-(6-morpholinyl-3-pyridazinyl)pyrido[2,3-d]pyrimidine dihydrochloride	morpholine	IR (KBr) 3600-3200, 3000, 1630, 1605, 1590, 1550 cm ⁻¹ ; MS m/z 464/466, 464.0829 (M+H) ⁺ ;

248	4-amino-5-(3-bromophenyl)-7-(6-pyrrolidinyl-3-pyridazinyl)pyrido[2,3-d]pyrimidine dihydrochloride	pyrrolidine	IR (KBr) 3600-3250, 3100-2800, 1640, 1605, 1560 cm ⁻¹ ; MS m/z 448/450, (M+H) ⁺ ;
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Examples 249-251

Following the procedures of Example 244, except in step (c) first substituting the appropriate reagent for R⁴ as indicated in Table 11B below for the R⁴ reagent of Example 5 244 step c, and secondly performing the condensation with ammonium acetate substituting dichloroethane as the solvent in place of the ethanol solvent in Example 244 step c, the compounds of Examples 249-251 were prepared. In some cases, the hydrochloride salts were not prepared.

10

Table 11BExamples 249-260

Ex. No.	Name	R ⁴ Reagent (for 7-position)	Analytical Data
249	4-amino-5-(3-bromophenyl)-7-(5-morpholinyl-2-pyrazinyl)pyrido[2,3-d]pyrimidine dihydrochloride	2-acetyl-5-morpholinyl-pyrazine	IR (KBr) 3478, 3058, 1562, 1542, 1378, 1306 cm ⁻¹ ; MS m/z 464/466, (M+H) ⁺ ;

250	4-amino-5-(3-bromophenyl)-7-(5-(N-(2-methoxyethyl)-N-methylamino)-2-pyrazinyl)pyrido[2,3-d]pyrimidine dihydrochloride	2-acetyl-5-(N-(2-methoxyethyl)-N-methylamino)-pyrazine	IR (KBr) 3482, 3299, 3053, 1612, 1540, 1310 cm ⁻¹ ; MS m/z 466/468, (M+H) ⁺ ;
251	4-amino-5-(3-bromophenyl)-7-(4-(morpholinylmethyl)-phenyl)pyrido[2,3-d]pyrimidine hydrochloride	1-((4-acetylphenyl)-methyl)-morpholine	IR (KBr) 3040, 1680, 1640, 1605, 1580, 1400 cm ⁻¹ ; MS m/z 466/468, (M+H) ⁺ ;

Example 252

4-amino-5-(3-bromophenyl)-7-(5-(N,N-bis(2-methoxyethyl)amino)-2-pyridinyl)pyrido[2,3-d]pyrimidine trihydrochloride

5

Step 252a. 1-(5-bromo-2-pyridyl)ethanone, ethylene ketal

A solution of dibromopyridine (5.2 g, 21.95 mmol), tributyl(1-ethoxyvinyl)tin (9.11 g, 25.24 mmol), Pd₂(dba)₃ (0.7 g, 0.8 mmol), and (2-furyl)P (0.37 g, 1.6 mmol) in 50 mL of toluene/THF (5:1) was warmed at reflux for 10 hours. The reaction mixture was concentrated, and the crude product was purified by elution through a short column of silica gel. The resulting enol-ether compound, ethylene glycol (2.79 g, 45 mmol), and p-toluenesulfonic acid (0.1 g) were dissolved in 50 mL of toluene and the solution was warmed at reflux for 10 hours. The reaction mixture was quenched by the addition of saturated aqueous NaHCO₃, and the aqueous layer was extracted with CH₂Cl₂. The combined organic layer was dried (Na₂SO₄), concentrated under reduced pressure, and the resulting crude product was purified by flash chromatography to provide the title compound (3.68 g, 79%).

Step 252b. 1-(5-(bis(2-methoxyethyl)amino)-2-pyridyl)ethanone

Following literature procedure (J. Org. Chem. 1996, 61, 720), a suspension of the compound from step 252a, bis(2-methoxyethyl)amine, t-BuONa, Pd₃(dba)₂, and BINAP 5 toluene was warmed at 80 °C for 8 hours. The reaction mixture was quenched by the addition of saturated aqueous NaHCO₃ and the aqueous layer was extracted with CH₂Cl₂. The combined organic layer was concentrated and the resulting residue was dissolved in 20 mL THF/3 M HCl (4:1) and stirred for 4 h. The reaction mixture was neutralized by the addition of 2 M NaOH (aq) and the aqueous layer was extracted with CH₂Cl₂. The 10 combined organic layer was dried, concentrated under reduced pressure, and the crude product was purified by flash chromatography to provide the title compound

Step 252c. 4-amino-5-(3-bromophenyl)-7-(5-(N,N-bis(2-methoxyethyl)amino)-2-pyridinyl)pyrido[2,3-d]pyrimidine trihydrochloride

15 Following the procedures of Example 244, except in step (c) first substituting the reagent from Step 252b for the R⁴ reagent of Example 244 step c, and secondly performing the condensation with ammonium acetate substituting dichloroethane as the solvent in place of the ethanol solvent in Example 244 step c, the free base of the title compound was prepared. The title compound was prepared from this by treatment with HCl in ether. IR 20 (KBr) 3440, 1635, 1605, 1580, 1360 cm⁻¹; MS m/z 466/468, (M+H)⁺.

Examples 253-260

Following the procedures of Example 244, except in step (c) first substituting the appropriate reagent for R⁴ as indicated in Table 11B below for the R⁴ reagent of Example 25 244 step c, and secondly performing the condensation with ammonium acetate substituting dichloroethane as the solvent in place of the ethanol solvent in Example 244 step c, the compounds of Examples 253-260 were prepared. In some cases, the hydrochloride salts were not prepared.

Ex. No.	Name	R ⁴ Reagent (for 7-position)	Analytical Data
253	4-amino-5-(3-bromophenyl)-7-(4-(imidazolylmethyl)-phenyl)pyrido[2,3-d]pyrimidine trihydrochloride	1-((4-acetylphenyl)-methyl)imidazole	IR (KBr) 3105, 1645, 1620, 1570, 1350 cm ⁻¹ ; MS m/z 466/468, (M+H) ⁺ ;
254	4-amino-5-(3-bromophenyl)-7-(5-(1-morpholinyl)-2-pyridinyl)pyrido[2,3-d]pyrimidine trihydrochloride	1-(5-morpholinyl-2-pyridyl)ethanone *	IR (KBr) 3297, 3081, 1646, 1564, 1494, 1362 cm ⁻¹ ; MS m/z 463/465, (M+H) ⁺ ;
255	4-amino-5-(3-bromophenyl)-7-(4-((dimethylamino)methyl)-phenyl)pyrido[2,3-d]pyrimidine dihydrochloride	1-(4-((dimethylamino)methyl)phenyl)ethanone	IR (KBr) 3308, 1645, 1590, 1560, 1375 cm ⁻¹ ; MS m/z 509/511, (M+H) ⁺ ;
256	4-amino-5-(3-bromophenyl)-7-(5-(4-hydroxy-1-piperidinyl)-2-pyridinyl)pyrido[2,3-d]pyrimidine dihydrochloride	1-(5-(4-hydroxypiperidinyl)-2-pyridyl)ethanone **	IR (KBr) 3000, 1650, 1600, 1580, 1550, 1400 cm ⁻¹ ; MS m/z 477/479, (M+H) ⁺ ;

257	4-amino-5-(3-bromophenyl)-7-(5-(N-formyl-N-methylamino)-2-pyridinyl)pyrido[2,3-d]pyrimidine dihydrochloride	5-acetyl-2-pyridinemethanamine	IR (KBr) 3477, 3060, 1678, 1638, 1566, 1495, 1319 cm ⁻¹ ; MS m/z 435/437, (M+H) ⁺ ;
258	4-amino-5-(3-bromophenyl)-7-(5-(2-propenyl)-2-pyridinyl)pyrido[2,3-d]pyrimidine	2-acetyl-5-(2-propenyl)-pyridine	IR (KBr) 3085, 1562, 1485, 1357 cm ⁻¹ ; MS m/z 418/420, (M+H) ⁺ ;
259	4-amino-5-(3-bromophenyl)-7-(3-(2-methoxyethyl)-2-oxo-6-benzoxazolyl)pyrido[2,3-d]pyrimidine hydrochloride	6-acetyl-3-(2-methoxyethyl)-benzoxazol-2-one	IR (KBr) 3440, 1770, 1625, 1605, 1580, 1360 cm ⁻¹ ; MS m/z 492/494, (M+H) ⁺ ;
260	4-amino-5-(3-bromophenyl)-7-(4-(1-(N-formylamino)-ethyl)phenyl)pyrido[2,3-d]pyrimidine	N-(1-(4-acetyl-phenyl)ethyl)-formamide	IR (KBr) 3283, 3054, 1678, 1631, 1547, 1352 cm ⁻¹ ; MS m/z 448/450, (M+H) ⁺ ;

* Prepared as in Ex. 252b, except substituting morpholine for the bis(2-methoxyethyl)amine thereof.

** Prepared as in Ex. 252b, except substituting 4-hydroxypiperidine for the bis(2-methoxyethyl)amine thereof.

Example 2614-amino-5-(3-pyridyl)-7-(4-dimethylamino)phenylpyrido[2,3-d]pyrimidine

The compound was prepared by using the method generally described above in Scheme 3 and the associated examples using 1-(4-dimethylaminophenyl)ethanone as the 5 R⁴ reagent (7-position) and nicotinaldehyde as the R³ reagent (5-position). 1R (cm-1) 3305.8, 2922, 1606, 1578, 1535, 1360. MS (M+H) 342.

Example 2624-(methylamino)-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine10 hydrochloride

The title compound was prepared by using the method described in Example 200, except substituting methylamine for the 2-(dimethylamino)ethylamine thereof. MS (M+H), 478 (1Br); IR (cm-1) 3455, 3047, 2959, 1580, 1351, 1234.

15 Example 2634-(2-methoxyethylamino)-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine hydrochloride

The title compound was prepared by using the method described in Example 200, except substituting 2-methoxyethylamine for the 2-(dimethylamino)ethylamine thereof. 20 MS (M+H), 522 (1Br); IR (cm-1) 3415, 2920, 1569, 1321, 1234.

Example 2644-amino-5-(3-bromophenyl)-7-(4-(1-methyl-2-imidazolyl)phenyl)pyrido[2,3-d]pyrimidine trihydrochloride

25

Step 264a. 1-(4-(1-Methylimidazol-2-yl)phenyl)ethanone

A solution of N-methyl imidazole (0.90 g, 11.0 mmol) in 12 mL of THF at -78 °C was treated with n-BuLi (7.5 mL, 1.6 M solution in hexanes, 12.0 mmol) for 0.5 hours at -78 °C. Next, ZnCl₂ (20 mL, 1.0 M solution in Et₂O, 20 mmol) was added, and the

30 solution was warmed to 25°C. To this solution was added Pd(PPh₃)₄ (70 mg, 0.06 mmol)

followed by 4-iodoacetophenone ethylene acetal (prepared from iodoacetophenone and ethylene glycol in the presence of an acid catalyst by standard procedures), and the reaction mixture was heated at reflux for 4 hours. The solution was then cooled to 25 °C and quenched by the addition of saturated aqueous NaHCO₃ (10 mL). The aqueous layer
5 was extracted with CH₂Cl₂, and the combined organic layer was concentrated under reduced pressure. The residue was dissolved in 30 mL of THF, 15 mL of 3 M aqueous HCl was added, and the mixture was stirred for 2 hours at 25 °C. The solution was neutralized by the addition of saturated aqueous NaHCO₃, and the aqueous layer was extracted with CH₂Cl₂. The combined organic layer was dried (MgSO₄) then
10 concentrated under reduced pressure. The crude product was purified by flash chromatography to provide the title compound (0.89 g, 64%).

Step 264b. 4-amino-5-(3-bromophenyl)-7-(4-(1-methyl-2-imidazolyl)phenyl)pyrido[2,3-d]pyrimidine trihydrochloride

15 Following the procedures of Example 244, except in step (c) first substituting the R⁴ reagent from Step 264a for the R⁴ reagent of Example 244 step c, and secondly performing the condensation with ammonium acetate substituting dichloroethane as the solvent in place of the ethanol solvent in Example 244 step c, the title compound was prepared. MS (M+H) 458 (1Br); IR (cm⁻¹) 3051, 2948, 1577, 1474, 1354.

20

Examples 265-267

Following the procedures of Example 244, except in step (c) first substituting the appropriate reagent for R⁴ as indicated in the Table below for the R⁴ reagent of Example 244 step c, and secondly performing the condensation with ammonium acetate substituting dichloroethane as the solvent in place of the ethanol solvent in Example 244 step c, the compounds of Examples 264-285 were prepared. In Ex. 266, the hydrochloride salt was not prepared.

Ex. No.	Name	R ¹ Reagent (for 7-position)	Analytical Data
265	4-amino-5-(3-bromophenyl)-7-(4-(aminomethyl)phenyl)pyrido[2,3-d]pyrimidine	1-(4-(aminomethyl)phenyl)ethanone	MS (M+H), 460; IR (cm-1) 3024, 2933, 1550, 1493, 1328
266	4-amino-5-(3-bromophenyl)-7-(2-bromo-4-(dimethylamino)phenyl)pyrido[2,3-d]pyrimidine	1-(2-bromo-4-(dimethylamino)phenyl)ethanone	MS (M+H), 500 (2 Br); IR (cm-1) 3049, 2949, 1536, 1468, 1320
267	4-amino-5-(3-bromophenyl)-7-(4-(dimethylaminoethyl)phenyl)pyrido[2,3-d]pyrimidine	1-(4-(dimethylaminoethyl)phenyl)ethanone	MS (M+H), 448 (1 Br); IR (cm-1) 3420, 3000, 2980, 1635, 1610, 1590, 1435, 1415

Example 268

4-amino-5-(3-bromophenyl)-7-(4-(3-(dimethylamino)propynyl)phenyl)pyrido[2,3-d]pyrimidine

5 A suspension of the compound of Example 63 (0.80 g, 1.59 mmol), PdCl₂(PPh₃)₂, CuI, and 3-dimethylaminoprop-1-yne in 20 mL of DMF/TEA (4:1) was heated at 50 °C for 3 hours. The volatiles were removed under reduced pressure, and the residue was purified by flash chromatography to provide the title compound (0.50 g, 68%). MS (M+H), 459 (1Br); IR (cm-1) 3027, 2964, 1513, 1470, 1360.

Examples 269-271

Following the procedures of Example 268, except substituting the reagent compound shown in the table below for the 3-dimethylaminoprop-1-yne of Example 268, the compounds shown in the table below were prepared.

5

Ex. No.	Name	Reagent	Analytical Data
269	4-amino-5-(3-bromophenyl)-7-(4-(3-amino-3-methylbutynyl)phenyl)pyrido[2,3-d]pyrimidine	1,1-dimethyl-propargyl amine	MS (M+H), 459 (1Br); IR (cm-1) 3041, 2967, 1562, 1484, 1319
270	4-amino-5-(3-bromophenyl)-7-(4-dimethylphosphonatophenyl)pyrido[2,3-d]pyrimidine	dimethyl phosphite	MS (M+H), 486 (1Br); IR (cm-1) 3105, 2912, 1625, 1437, 1350
271	4-amino-5-(3-bromophenyl)-7-(4-(3-(methoxypropynyl)pyrido[2,3-d]pyrimidine	methyl propargyl ether	MS (M+H), 446 (1Br); IR (cm-1) 3053, 2929, 1560, 1484, 1352

Example 2724-amino-5-(3-bromophenyl)-7-(4-carboxyphenyl)pyrido[2,3-d]pyrimidine

A solution of 4-amino-5-(3-bromophenyl)-7-(4-cyanophenyl)pyrido[2,3-d]pyrimidine (the compound of Example 37, (0.47 g, 1.17 mmol) in 15 mL of 6 M HCl (aqueous) was heated at 60 °C for 8 hours. The mixture was lyophilized and the crude product was purified by flash chromatography to provide the title compound (0.14 g, 28%). MS (M+H), 422 (1Br); IR (cm-1) 3064, 2628, 1692, 1403, 1273.

10

Example 2734-amino-5-(3-bromophenyl)-7-(4-methyl-3-oxo-2H-4H-pyrido[3,2-b]-1,4-oxazinyl)pyrido[2,3-d]pyrimidine

5

Step 273a. 7-acetyl-2H-pyrido[3,2-b]-1,4-oxazin-3(4H)-one

A solution of 2H-pyrido[3,2-b]-1,4-oxazin-3(4H)-one (9.8 g, 65.27 mmol, Aldrich) in 120 mL of THF/MeOH (5:1) was treated with 0.4 mL of concentrated HCl (aqueous) followed by N-bromosuccinimide (17.8 g, 100 mmol) in several portions over 10 minutes. After 12 hours at 25 °C the reaction mixture was quenched by the addition of saturated aqueous NaHSO₃. The aqueous layer was extracted with CH₂Cl₂ and the combined organic layer was dried (Na₂SO₄), concentrated under reduced pressure, and purified by flash chromatography to provide 7-bromo-2H-pyrido[3,2-b]-1,4-oxazin-3(4H)-one (8.4 g, 56%). A mixture of 7-bromo-2H-pyrido[3,2-b]-1,4-oxazin-3(4H)-one (3.2 g, 14 mmol), tributyl(1-ethoxyvinyl)tin (6.1 g, 17 mmol), Pd₂(dba)₃ (0.5 g, 0.56 mmol), and (2-furyl)₃P (0.3 g, 1.2 mmol) in 30 mL of toluene/THF (5:1) was warmed at reflux for 10 hours. The reaction mixture was concentrated under reduced pressure, and the residue was dissolved in 50 mL of THF. 15 mL of 4 M HCl (aqueous) was added, and the mixture was stirred for 4 hours at 25 °C. The solution was neutralized by the addition of NaHCO₃ (aqueous), and the aqueous layer was extracted with CH₂Cl₂. The combined organic layer was dried (Na₂SO₄), concentrated, and the crude product was purified by flash chromatography to provide 7-acetyl-2H-pyrido[3,2-b]-1,4-oxazin-3(4H)-one (2.37 g, 88%). MS (M+H), 463 (1 Br); IR (cm⁻¹) 3400, 3200-2800, 1700, 1640, 1605, 1590, 1395, 1380, 1345.

25

Step 273b. 7-acetyl-4-methyl-2H-pyrido[3,2-b]-1,4-oxazin-3(4H)-one

The compound from step 273 a was treated with methyl iodide and NaH in 1:1 THF/DMF for 6 hours at 0 °C to 25 °C. The reaction was quenched with aqueous sodium

bicarbonate solution, the mixture was extracted with dichloromethane, and the residue was purified by chromatography to give the title compound. MS (M+H), 407.

Step 273c. 4-amino-5-(3-bromophenyl)-7-(4-methyl-3-oxo-2H-4H-pyrido[3,2-b]-1,4-oxazinyl)pyrido[2,3-d]pyrimidine

Following the procedure of Example 244 Step c, except first substituting 7-acetyl-4-methyl-2H-pyrido[3,2-b]-1,4-oxazin-3(4H)-one (the R⁴ reagent) from Step 273b for the R⁴ reagent of Example 244 Step c, and secondly performing the condensation with ammonium acetate substituting dichloroethane as the solvent in place of the ethanol
10 solvent in Example 244 step c, the title compound was prepared. MS (M+H), 463 (1 Br); IR (cm⁻¹) 3400, 3200-2800, 1700, 1640, 1605, 1590, 1395, 1380, 1345.

Example 274

4-amino-5-(3-bromophenyl)-7-(4-(2-(dimethylamino)ethyl)-3-oxo-2H-4H-pyrido[3,2-b]-1,4-oxazin-7-yl)pyrido[2,3-d]pyrimidine

Step 274a. 7-acetyl-4-dimethylaminoethyl -2H-pyrido[3,2-b]-1,4-oxazin-3(4H)-one
The compound from Example 273 Step a was treated with 2-chloro-(N,N-dimethyl)ethylamine HCl and K₂CO₃ in aqueous acetone at reflux. The mixture was
20 diluted with water and extracted with dichloromethane, and the residue was purified by chromatography to give the title compound.

Step 274b. 4-amino-5-(3-bromophenyl)-7-(4-(2-(dimethylamino)ethyl)-3-oxo-2H-4H-pyrido[3,2-b]-1,4-oxazin-7-yl)pyrido[2,3-d]pyrimidine

25 Following the procedures of Example 244 Step c, except in step c first substituting 7-acetyl-4-dimethylaminoethyl -2H-pyrido[3,2-b]-1,4-oxazin-3(4H)-one (the R⁴ reagent, from Step 273b) for the R⁴ reagent of Example 244 Step c, and secondly performing the condensation with ammonium acetate substituting dichloroethane as the solvent in place of the ethanol solvent in Example 244 step c, the title compound was prepared. MS (M+H),
30 519 (1 Br); IR (cm⁻¹) 3440, 1685, 1630, 1605, 1580, 1395

Example 275 .4-amino-5-(3-bromophenyl)-7-(2,3-dihydro-3-(dimethylaminoethyl)-2-oxobenzoxazol-6-yl)pyrido[2,3-d]pyrimidine

5

Step 275a. 6-acetyl-2-benzoxazolinone

Following the procedures of Example 273 Step a, except substituting 2-benzoxazolinone (Aldrich) for the 2H-pyrido[3,2-b]-1,4-oxazin-3(4H)-one thereof, the title compound was prepared.

10

Step 275b. 6-acetyl-3-(dimethylaminoethyl)-2-benzoxazolinone

The compound from Example 275 Step a was treated with 2-chloro-(N,N-dimethyl)ethylamine HCl and K₂CO₃ in aqueous acetone at reflux. The mixture was diluted with water and extracted with dichloromethane, and the residue was purified by chromatography to give the title compound.

Step 275c. 4-amino-5-(3-bromophenyl)-7-(2,3-dihydro-3-(dimethylaminoethyl)-2-oxobenzoxazol-6-yl)pyrido[2,3-d]pyrimidine

Following the procedures of Example 244 Step c, except in step c first substituting the compound from Step 275a for the R⁴ reagent of Example 244 Step c, and secondly performing the condensation with ammonium acetate substituting dichloroethane as the solvent in place of the ethanol solvent in Example 244 step c, the title compound was prepared. MS (M+H), 506 (1 Br); IR (cm⁻¹) 3400, 3050, 1630, 1610, 1360.

Example 2764-amino-5-(3-bromophenyl)-7-(4-methyl-3-oxo-2H-4H-benzo-1,4-oxazin-7-yl)pyrido[2,3-d]pyrimidine5 Step 276a. 6-acetyl-3-methyl-2-benzoxazolinone

The compound from Example 275 Step a was treated with methyl iodide and NaH in 1:1 THF/DMF for 6 hours at 0 °C to 25 °C. The reaction was quenched with aqueous sodium bicarbonate solution, the mixture was extracted with dichloromethane, and the residue was purified by chromatography to give the title compound.

10

Step 276b. 1-(3-hydroxy-4-methylaminophenyl)-ethanone

The compound from Step 276a (1.60 g, 8.37 mmol) was dissolved in acetone (70 mL) and treated with 1M aqueous K₂CO₃ solution (25 mL) with heating at reflux overnight. The mixture was neutralized with acid, then extracted with diethyl ether. The solvent was dried (MgSO₄) and removed under vacuum to give the title compound (2.01 g)

Step 276c. 7-acetyl-4-methyl-2H-4H-benzo-1,4-oxazin-3-one

The compound from Step 276b (2.01 g, 8.37 mmol) was dissolved in DMSO and treated with sodium ethoxide (8.4 mmol) and bromoacetic acid (1.40 g, 8.4 mmol) at room temperature overnight. The mixture was diluted with water and ether, and the title compound was isolated by filtration (0.48 g). MS (M+H), 206.

25 Step 276d. 4-amino-5-(3-bromophenyl)-7-(4-methyl-3-oxo-2H-4H-benzo-1,4-oxazin-7-yl)pyrido[2,3-d]pyrimidine

Following the procedures of Example 244 Step c, except in step c first substituting the compound from Step 276c for the R⁴ reagent of Example 244 Step c, and secondly performing the condensation with ammonium acetate substituting dichloroethane as the solvent in place of the ethanol solvent in Example 244 step c, the title compound was

prepared. MS (M+H), 462 (1 Br); IR (cm⁻¹) 3500, 2800-3200, 1690, 1645, 1610, 1590, 1385, 1355.

Example 277

5 4-amino-5-(3-bromophenyl)-7-(2,2,4-trimethyl-3-oxo-2H-4H-benzo-1,4-oxazin-7-
y)pyrido[2,3-d]pyrimidine

Step 277a. 7-acetyl-2,2,4-trimethyl-2H-4H-benzo-1,4-oxazin-3-one

The compound from Step 276b (2.25 g, 9 mmol) was dissolved in DMSO and
10 treated with sodium ethoxide (9 mmol) and 2-bromo-2-methylpropanoic acid (1.76 g, 9
mmol) at room temperature overnight. The mixture was diluted with water, and the
mixture was extracted with ether:ethyl acetate. The extract was dried (MgSO₄), the
solvent was removed under vacuum, and the residue was purified by chromatography
(silica gel) to give the title compound (1.33 g) MS (M+H), 234.

15

Step 277b. 4-amino-5-(3-bromophenyl)-7-(2,2,4-trimethyl-3-oxo-2H-4H-benzo-1,4-
oxazin-7-yl)pyrido[2,3-d]pyrimidine

Following the procedures of Example 244 Step c, except in step c first substituting
the compound from Step 277a for the R⁴ reagent of Example 244 Step c, and secondly
20 performing the condensation with ammonium acetate substituting dichloroethane as the
solvent in place of the ethanol solvent in Example 244 step c, the title compound was
prepared. MS (M+H), 490 (1 Br); IR (cm⁻¹) 3450, 2900-3100, 1680, 1645, 1610, 1515,
1385, 1365, 1165.

25

Example 278

4-amino-5-cyclohexyl-7-(4-(2-dimethylamino)ethyl)-2H-4H-benzo-3-oxo-1,4-oxazin-7-
y)pyrido[2,3-d]pyrimidine

Step 278a. 1-(3-hydroxy-4-(dimethylamino)ethyl)phenyl)-ethanone

A sample of 6-acetyl-3-(dimethylaminoethyl)-2-benzoxazolinone (from Example 275 Step b) was dissolved in acetone and treated with 1M aqueous K_2CO_3 solution with heating at reflux overnight. The mixture was neutralized with acid, then extracted with diethyl ether. The solvent was dried ($MgSO_4$) and removed under vacuum to give the title compound.

Step 278b. 7-acetyl-4-(dimethylamino)ethyl)-2H-4H-benzo-1,4-oxazin-3-one

A sample of the compound from Step 278a (8.94 g, 32 mmol) was dissolved in 10 DMSO and treated with sodium ethoxide (32 mmol) and bromoacetic acid (5.34 g, 32 mmol) at room temperature for 2 days. The mixture was diluted with water then extracted with ether. The extract was dried ($MgSO_4$), the solvent was removed under vacuum, and the residue was purified by chromatography (silica gel) to give the title compound (1.94 g). MS (M+H), 263.

15

Step 278c. 4-amino-5-cyclohexyl-7-(4-(dimethylamino)ethyl)-2H-4H-benzo-3-oxo-1,4-oxazin-7-yl]pyrido[2,3-d]pyrimidine

Following the procedures of Example 244 Step c, except in step c first substituting 1,1-dicyano-3-cyclohexylethene (prepared according to the method of Moison, et al. 20 (Tetrahedron (1987), 43:537-542) by treating cyclohexane carboxaldehyde with malononitrile in the presence of finely powdered magnesium oxide in dichloromethane) for the R₃ reagent of Example 244 Step c, and substituting the compound from Step 278b for the R⁴ reagent of Example 244 Step c, and also performing the condensation with ammonium acetate but also substituting dichloroethane as the solvent in place of the 25 ethanol solvent in Example 244 step c, the title compound was prepared. MS (M+H) 447; IR(cm⁻¹) 3400, 2900, 1690, 1610, 1590, 1395.

Example 2794-amino-5-(3-bromophenyl)-7-(5-(1-methylethyl)-2-pyridyl)pyrido[2,3-d]pyrimidineStep 279a. 1-(5-methylethyl-2-pyridyl)ethanone

5 A solution of 2-acetyl-5-bromopyridine (1.45 g, 7.9 mmol), 2-propenyltrimethyltin (1.77 g, 8.7 mmol), $\text{Pd}_2(\text{dba})_3$ (0.33 g, 0.36 mmol), and tri-2-furylphosphine (0.17 g, 0.72 mmol) in 25 mL of benzene was warmed at 60 °C for 4 hours. The reaction mixture was concentrated and the coupled product was purified by flash chromatography (1.22 g, 96 %). The product was dissolved in 25 mL of EtOH and the solution was purged with a
10 stream of H_2 . 10% Palladium on charcoal (50 mg) in 0.5 mL of EtOH was added and the reaction mixture was stirred for 12 h under an atmosphere of H_2 . The reaction mixture was filtered and the resulting solution was concentrated under reduced pressure. The title compound, 2, (1.04 g, 84%) was isolated following flash chromatography.

15 Step 279b. 4-amino-5-(3-bromophenyl)-7-(5-(1-methylethyl)-2-pyridyl)pyrido[2,3-d]pyrimidine

Following the procedures of Example 244 Step c, except in step c substituting the compound from Step 279a for the R^4 reagent of Example 244 Step c, and performing the condensation with ammonium acetate and also substituting dichloroethane as the solvent
20 in place of the ethanol solvent in Example 244 step c, the title compound was prepared.
MS ($\text{M}+\text{H}$) 421 (1Br); IR (cm-1) 3489, 2940, 1545, 1482, 1357.

Examples 280-281

25 Following the procedures of Example 244 Step c, except in step c substituting the compound shown below for the R^4 reagent of Example 244 Step c, and performing the condensation with ammonium acetate and also substituting dichloroethane as the solvent in place of the ethanol solvent in Example 244 step c, the compounds shown in the table below were prepared.

Ex. No.	Name	R ⁴ Reagent (for 7-position)	Analytical Data
280	4-amino-5-(3-bromophenyl)-7-(5-piperidin-1-ylpyrid-2-yl)pyrido[2,3-d]pyrimidine	1-(5-piperidinyl-2-pyridyl)ethanone *	MS (M+H), 460 (1Br); IR (cm-1) 3064, 2937, 1556, 1493, 1358
281	4-amino-5-(1-(4-bromophenyl)ethyl)-7-(6-morpholinylpyrid-3-yl)pyrido[2,3-d]pyrimidine	1-(2-morpholinyl-5-pyridyl)ethanone **	MS (M+H), 491 (1 Br); IR (cm-1) 1585, 1555, 1505, 1240, 1110, 940

* Prepared as in Ex. 252b, except substituting morpholine for the bis(2-methoxyethyl)amine thereof.

** prepared by treatment of 5-acetyl-2-chloro-pyridine with morpholine in refluxing ethanol.

5

Example 282

4-amino-5-(3-bromophenyl)-7-(4-((N-formylamino)methyl)phenyl)pyrido[2,3-d]pyrimidine

Step 282a. 4-cyanoacetophenone, acetal with 2,2-dimethylpropylene glycol

A sample of 4-cyanoacetophenone (4.35 g, 30 mmol) was dissolved in 150 mL of hexanes, and to this solution were added 2,2-dimethylpropylene glycol (3.44 g, 33 mmol) and a catalytic amount (10 mg) of p-toluene sulfonic acid. The reaction was heated overnight at reflux with a Dean-Stark trap, and an additional portion of glycol (33 mmol) was added. The reaction was continued for 3 hours, then cooled and the solvent was removed. The residue was dissolved in ethyl acetate, and this solution was washed with aqueous NaHCO₃, water and brine, and dried over MgSO₄. The solvent was removed under vacuum to give the title compound (7.46 g).

Step 282b. 4-(aminomethyl)acetophenone, acetal with 2,2-dimethylpropylene glycol

The compound from Step 282a (2.31 g, 10 mmol) was dissolved in ether (50 mL) and stirred with lithium aluminum hydride (0.76 g, 20 mmol) at ambient temperature 5 overnight. The reaction was quenched with MgSO₄•10 H₂O, and the mixture was diluted with ether. The mixture was filtered, and the filtrate removed to give the title compound.

Step 282c. 1-(4-(BOC-aminomethyl)phenyl)ethanone

The compound from Step 282b (1.18 g, 5 mmol) was dissolved in THF (20 mL), 10 1N HCl (20 mL) was added, and the mixture was stirred for 2 days. The volatiles were removed under vacuum, the residue was dissolved in THF (20 mL), and d-tibutyl dicarbonate (2.18 g, 10 mmol) was added. The mixture was stirred at room temperature over a weekend. The solution was diluted with water, and the mixture was extracted with ether and ethyl acetate. The organic extracts were dried (MgSO₄), and the solvent was 15 remove under vacuum to give the title compound.

Step 282d. 4-amino-5-(3-bromophenyl)-7-(4-(N-formylamino)methyl)phenyl)pyrido[2,3-d]pyrimidine

Following the procedures of Example 244, except in step c substituting the 20 compound from Step 282c for the R⁴ reagent of Example 244 Step c, and performing the condensation with ammonium acetate but also substituting dichloroethane as the solvent in place of the ethanol solvent in Example 244 step c, the title compound was prepared. MS (M+H) 434 (1 Br); IR (cm⁻¹) 3440, 2700-3150, 1635, 1580, 1380.

25

Example 2834-amino-5-(3-bromophenyl)-7-(4-(1-(N-methylamino)-1-methylethyl)phenyl)pyrido[2,3-d]pyrimidine

Step 283a. 4-(1-amino-1-methylethyl)acetophenone

5 CeCl_3 (10 g, 34.9 mmol) was suspended in THF (60 mL), and the mixture was cooled to -78 °C. Methyl lithium (1.4 M, 2 mL) was added, and the mixture was stirred for 20 minutes. Then the compound from Example 282 Step a, (4-cyanoacetophenone acetal with 2,2-dimethylpropylene glycol, 2.31 g, 10 mmol) in 2 mL of THF was added. After stirring for 4 hours, the mixture was allowed to warm to room temperature while stirring for 16 hours. The reaction was quenched with water and ammonium hydroxide, filtered, and the filtrate was extracted with dichloromethane. The solution was dried (MgSO_4), and the solvent was removed to give the title compound.

10

Step 283b. 4-(1-(N-BOC-amino)-1-methylethyl)acetophenone

The compound from Step 283a (2.32 g, 8.77 mmol) was treated sequentially with HCl and di-t-butyl dicarbonate according to the procedure of Example 282 Step c to give the title compound (1.60 g). MS (M+H) 278.

15

Step 283c. 4-amino-5-(3-bromophenyl)-7-(4-(1-(N-formylamino)-1-methylethyl)phenyl)pyrido[2,3-d]pyrimidine

20 Following the procedures of Example 244 Step c, except in step c substituting the compound from Step 283b for the R^4 reagent of Example 244 Step c, and performing the condensation with ammonium acetate but also substituting dichloroethane as the solvent in place of the ethanol solvent in Example 244 step c, the title compound was prepared. MS (M+H) 462 (1 Br); IR (cm-1) 3440, 1640, 1605, 1580, 1380.

25

Example 2844-amino-5-(3-bromophenyl)-7-(4-(1-(N,N-dimethylamino)-1-methylethyl)phenyl)pyrido[2,3-d]pyrimidine

Step 284a. 4-(1-(dimethylamino)-1-methylethyl)acetophenone

The compound from Step 283a (1.18 g, 5 mmol) was dissolved in 5 mL formic acid, and 5 mL of formalin (37%) was added. The mixture was heated at reflux for 4 hours, then cooled and neutralized with 2N Na₂CO₃. The mixture was extracted with dichloromethane. The solution was dried (MgSO₄), and the solvent was removed to give the title compound (0.94 g). MS (M+H) 462 (1 Br); IR (cm⁻¹) 3520, 1640, 1610, 1580, 1375.

10

Examples 285-286

Following the procedures of Example 157, except substituting the appropriate reagents for the R³ and R⁴ reagents of Example 157 as indicated in the Table below, compounds of Examples 285-286 were prepared. For Example 286, treatment with aqueous HCl was omitted, and the free base 15 was obtained.

Examples 285-286

Ex. No.	Name	R ³ Reagent (for 5-position)	R ⁴ Reagent (for 7-position)	Analytical Data
285	4-amino-5-(3-bromophenyl)-7-(N-acetyl-5-indolinyl)pyrido[2,3-d]pyrimidine	1,1-dicyano-(3-(3-bromophenyl)propene	1-(N-acetyl-5-indolinyl)-ethanone	mp (hydrochloride salt) >270°C. IR (cm ⁻¹) 3445, 3100-2500, 1640, 1605, 1445, 1395, 1325. LRMS [M+H] ⁺ m/z 460, 462.

286	4-amino-5-cyclohexyl-7-(6-chloro-3-pyridyl)pyrido[2,3-d]pyrimidine	1,1-dicyano-3-cyclohexylethene	1-(6-chloro-3-pyridyl)-ethanone	mp 240-242 °C. IR (cm-1) 3528, 3300, 3086, 2936, 2853, 1645, 1590, 1575, 1565, 1350. LRMS [M+H] ⁺ m/z 340.
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Examples 287-300

Following the procedures of Example 157, except substituting the appropriate R³ and R⁴ reagents as indicated in the Table below and replacing the formamide or formamidine acetate treatment with treatment with triethyl orthoformate at reflux in the presence of a catalytic amount of ammonium sulfate, followed by cooling to 25 °C and addition of excess ammonia in ethanol, compounds of Examples 287-300 were prepared. After 24 hours, the precipitated amidine compound was filtered and washed with hexanes, then dried under vacuum. The amidine compound was then heated in 1,2-dichloroethane at reflux for 1-8 hours. The reaction mixture was cooled to room temperature and purified by chromatography, and the product was recrystallized if necessary. The treatment with aqueous HCl was omitted in some cases, and the free bases were obtained.

15

Examples 287-300

Ex. No.	Name	R ³ Reagent (for 5-position)	R ⁴ Reagent (for 7-position)	Analytical Data
287	4-amino-5-(1-(2-bromophenyl)ethyl)-7-(6-dimethylamino-3-pyridyl)pyrido[2,3-d]pyrimidine	1,1-dicyano-2-methyl-(3-(2-bromophenyl)propene	1-(6-dimethylamino-3-pyridyl)-ethanone	IR (cm-1) 2600-3500, 1650, 1602, 1596, 1520 cm-1. LRMS [M+H] ⁺ m/z 449, 451.

288	4-amino-5-(1-(2-bromophenyl)ethyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine	1,1-dicyano-2-methyl-(3-(2-bromophenyl)propene	1-(6-morpholinyl-3-pyridyl)-ethanone	mp (dihydrochloride salt) 213-216 °C. IR (cm ⁻¹) 2400-3500, 1660, 1600. LRMS [M+H] ⁺ m/z 491 & 493.
289	4-amino-5-(1-(2-bromophenyl)ethyl)-7-(6-(N-methyl-N-formyl)amino)-3-phenyl)pyrido[2,3-d]pyrimidine	1,1-dicyano-2-methyl-(3-(2-bromophenyl)propene	1-(6-(N-methyl-N-formyl)amino)-3-pyridyl)-ethanone	mp 252-253°C. IR (cm ⁻¹) 3515, 3310, 3200-2800, 1675, 1585, 1560, 1545, 1340. LRMS [M+H] ⁺ m/z 462, 464.
290	4-amino-5-cyclohexyl-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine	1,1-dicyano-3-cyclohexylethen	1-(6-morpholinyl-3-pyridyl)-ethanone	mp (dihydrochloride salt) 208-210. IR (cm ⁻¹) 3490, 3300, 3050-3250, 1620, 1580, 1550, 1490. LRMS [M+H] ⁺ m/z 391.

291	4-amino-5-((2-bromophenyl)methyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine	1,1-dicyano-(3-(2-bromophenyl)propene	1-(6-morpholinyl-3-pyridyl)-ethanone	mp (dihydrochloride salt) 201-204 °C. IR (cm-1) 3601, 3500, 3310, 2960, 2850, 1585, 1561, 1502, 1345 . LRMS [M+H] ⁺ m/z 477, 479.
292	4-amino-5-(4-tetrahydropyranyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine	1,1-dicyano-3-(4-tetrahydropyranyl)ethene *	1-(6-morpholinyl-3-pyridyl)-ethanone	mp (dihydrochloride salt) 213-216 °C. IR (cm-1) 3310, 3060, 2955, 1587, 1559, 1506, 1350. LRMS [M+H] ⁺ m/z 393.
293	4-amino-5-cyclohexyl-7-(6-dimethylamino-3-pyridyl)pyrido[2,3-d]pyrimidine	1,1-dicyano-3-cyclohexylethene	1-(6-dimethylamino-3-pyridyl)-ethanone	mp (dihydrochloride salt) 272-274 °C. IR (cm-1) 3532, 3294, 3100, 2930, 2853, 1606, 1586, 1560, 1522, 1387. LRMS [M+H] ⁺ m/z 349.

294	4-amino-5-(1-ethylpropyl)-7-(6-dimethylamino-3-pyridyl)pyrido[2,3-d]pyrimidine	1,1-dicyano-3-ethylpentene	1-(6-dimethylamino-3-pyridyl)-ethanone	mp (free base): 223.5-225 °C. IR (cm ⁻¹) 3480, 3000-3470, 2800-3000, 1630, 1610, 1580, 1565, 1520. LRMS [M+H] ⁺ m/z 337.
295	4-amino-5-cyclopentyl-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine	1,1-dicyano-3-cyclopentylethen	1-(6-morpholinyl-3-pyridyl)-ethanone	IR (cm ⁻¹) 3495, 3320, 3080, 2950, 1645, 1600, 1500, 1400, 1350, 1240. LRMS [M+H] ⁺ m/z 377.
296	4-amino-5-cyclohexyl-7-(2-chloro-3-pyridyl)pyrido[2,3-d]pyrimidine	1,1-dicyano-3-cyclohexylethen	1-(2-chloro-3-pyridyl)-ethanone	IR (cm ⁻¹) 3305, 3155, 2930, 2855, 1590, 1610, 1590, 1545, 1345. LRMS [M+H] ⁺ m/z 340, 342.
297	4-amino-5-(3,5-dimethylcyclohexyl)-7-(6-dimethylamino-3-pyridyl)pyrido[2,3-d]pyrimidine	1,1-dicyano-3-(3,5-dimethylcyclohexyl)ethene	1-(6-dimethylamino-3-pyridyl)-ethanone	IR (cm ⁻¹) 3310, 3100, 2950, 1605, 1590, 1555, 1390, 1350. LRMS [M+H] ⁺ m/z 377.

298	4-amino-5-((N-(benzyloxycarbonyl)-4-piperidinyl)methyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine	1,1-dicyano-(3-(4-(benzyloxycarbonyl)piperidin-1-yl)propene	1-(6-morpholinyl-3-pyridyl)-ethanone	IR (cm-1) 3538, 3311, 3032, 2925, 2852, 1696, 1585, 1560. LRMS [M+H] ⁺ m/z 540.
299	4-amino-5-cyclohexyl-7-(6-bromo-3-pyridyl)pyrido[2,3-d]pyrimidine	1,1-dicyano-3-cyclohexylethene	1-(6-bromo-3-pyridyl)-ethanone	m.p. 250-252 °C, IR (cm-1) 3530, 3298, 3093, 2932, 2856, 1645, 1583, 1569, 1543, 1461, 1346. LRMS [M+H] ⁺ 384, 386.
300	4-amino-5-cyclohexyl-7-(3-cyanophenyl)pyrido[2,3-d]pyrimidine	1,1-dicyano-3-cyclohexylethene	1-(3-cyanophenyl)-ethanone	m. p. 223-224 °C. IR (cm-1) 3528, 3298, 3075, 2937, 2235, 1645, 1586, 1548, 1567, 1463. LRMS [M+H] ⁺ 332.

* The 1,1-dicyano-3-cyclohexylethene was prepared according to the method of Moison, et al. (Tetrahedron (1987), 43:537-542) by treating cyclohexane carboxaldehyde with malononitrile in the presence of finely powdered magnesium oxide in dichloromethane.

5

The reagents for the following examples were prepared by this method substituting the compound shown below for the cyclohexane carboxaldehyde used to prepare the reagent of Example 290.

Example 292, tetrahydropyran-4-carboxaldehyde;

Example 294, 2-ethylbutanaldehyde;

Example 295, cyclopentane carboxaldehyde;
 Example 297, 3,5-dimethylcyclohexane carboxaldehyde;
 Example 298, N-(phenylmethoxylcarbonyl)piperidine-4-carboxaldehyde
 (this material was prepared from N-(carbobenzyloxy)-4-(2-hydroxyethyl)piperidine
 5 (Brehm et al., *Helv.Chim.Acta*, 70; (1987), 1981-1987 by treatment with TEMPO
 (2,2,6,6-tetramethylpiperidinyloxy radical) and potassium bromide in
 dichloromethane at 0 °C to which was added commercial bleach (Clorox)
 containing sodium bicarbonate).

10

Examples 301-305

Following the procedures of Example 246, except in step (c) substituting the appropriate reagents for methylamine as indicated in the Table below to prepare the correct R⁴ reagent, and substituting the R³ reagent shown below for the R³ reagent of Example 246 step d, the compounds of Examples 301-305 were prepared. For Example 15 302 only, the condensation solvent was DMSO instead of ethanol and dimethoxyethane.

Examples 301-305

Ex. No.	Name	R ³ reagent	reagent of step c	Analytical Data
301	4-amino-5-(1-(2-bromophenyl)ethyl)-7-(6-dimethylamino-3-pyridazinyl)pyrido[2,3-d]pyrimidine	1,1-dicyano-(3-(2-bromophenyl)propene	dimethylamine	mp (dihydrochloride salt) >220°C. IR (cm ⁻¹) 3500-2400, 1640, 1610, 1580, 1370. LRMS [M+H] ⁺ m/z 450, 452.

302	4-amino-5-(3-bromophenyl)-7-(6-imidazolyl-3-pyridazinyl)pyrido[2,3-d]pyrimidine	1',1'-dicyano-(3-bromostyrene	imidazole sodium salt	mp (tetrahydrochloride salt) >240°C. IR (cm ⁻¹) 3600-2400, 1640, 1610, 1590, 1560, 1415, 1370. LRMS [M+H] ⁺ m/z 445, 447.
303	4-amino-5-(3-bromophenyl)-7-(6-(azacycloheptanyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine	1',1'-dicyano-(3-bromostyrene	azacycloheptane	mp (dihydrochloride salt) >190°C. IR (cm ⁻¹) 3435, 3100-2400, 1635, 1610, 1590, 1550, 1440, 1370. LRMS [M+H] ⁺ m/z 476, 478.
304	4-amino-5-(3-bromophenyl)-7-(6-(N-methyl-N-(1-methylethyl))amino)-3-pyridazinyl)pyrido[2,3-d]pyrimidine	1',1'-dicyano-(3-bromostyrene	N-methyl-N-(1-methylethyl)amine	mp (dihydrochloride salt) >210°C. IR (cm ⁻¹) 3435, 3100-2400, 1635, 1610, 1590, 1550, 1410, 1370. LRMS [M+H] ⁺ m/z 450, 452.

305	4-amino-5-(1-(2-bromophenyl)ethyl)-7-(6-morpholinyl-3-pyridazinyl)pyrido[2,3-d]pyrimidine	1,1-dicyano-(3-(2-bromophenyl)propene	morpholine	IR (cm-1) 3475, 3313, 3100, 1650, 1620, 1580, 1555. LRMS [M+H] ⁺ at 492, 494.
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Example 3064-amino-5-cyclohexyl-7-(6-(4-acetyl)piperazinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine

5 A mixture of 679 mg (2 mmol) of the compound from Example 298 and 1.28 g (10 mmol) of N-acetyl piperazine in 5 mL of DMSO was heated at 110 °C for 5 hours. On cooling a precipitate was deposited, which was collected and washed with 20% methanol and dried to give 647 mg of the product as orange flakes: IR (cm-1) 3522, 3306, 3110, 2925, 2854, 1670, 1650, 1586, 1506. LRMS [M+H]⁺ m/z 432.

10

Examples 307-322

Follwing the procedure of Example 306, except substituting the reagent shown in the table below for the N-acetyl piperazine of Example 306, the compounds shown in the table were prepared. The compounds were purified by 15 HPLC chromatography.

Ex. No.	Name	reagent	Analytical Data

307	4-amino-5-cyclohexyl-7-(6-(4-acetyl-1,4-diazacycloheptanyl)-3-pyridyl)pyrido[2,3-d]pyrimidine	1-acetyl-1,4-diazacycloheptane	m.p. 169-171 °C, IR (cm ⁻¹) 3535, 3309, 3096, 2930, 2854, 1638, 1605, 1587, 1558, 1513. LRMS [M+H] ⁺ 446.
308	4-amino-5-cyclohexyl-7-(6-(4-methyl-1,4-diazacycloheptanyl)-3-pyridyl)pyrido[2,3-d]pyrimidine	1-methyl-1,4-diazacycloheptane	LRMS [M+H] ⁺ 419.
309	4-amino-5-cyclohexyl-7-(6-(N-methyl-N-(2-(2-pyridyl)ethyl)amino)-3-pyridyl)pyrido[2,3-d]pyrimidine	N-methyl-N-(2-(2-pyridyl)ethyl)amine	LRMS [M+H] ⁺ 441.
3101	4-amino-5-cyclohexyl-7-(6-2-(N-(N',N'-dimethylaminoethyl)-N-methylamino)-3-pyridyl)pyrido[2,3-d]pyrimidine	N,N-dimethyl, N'-methyl-1,2-ethylenediamine	LRMS [M+H] ⁺ 421.

311	4-amino-5-cyclohexyl-7-(6-azetidinyl-3-pyridyl)pyrido[2,3-d]pyrimidine	azetidine	LRMS [M+H] ⁺ 361.
312	4-amino-5-cyclohexyl-7-(6-(3-(N-methylacetamido)pyrrolidinyl)pyridyl)pyrido[2,3-d]pyrimidine	N-methyl-N-(3-pyrrolidinyl)acetamide	LRMS [M+H] ⁺ 447.
313	4-amino-5-cyclohexyl-7-(6-(3-(formamido)pyrrolidinyl)pyridyl)pyrido[2,3-d]pyrimidine	pyrrolidine-2-formamide	LRMS [M+H] ⁺ 419.
314	4-amino-5-cyclohexyl-7-(4-oxo-1-phenyl-1,3,8-triazaspiro[4.5]decan-8-yl)pyrido[2,3-d]pyrimidine	1-phenyl-1,38-triazaspiro[4.5]decan-4-one	LRMS [M+H] ⁺ 536.
315	4-amino-5-cyclohexyl-7-(6-(2-(methoxymethyl)pyrrolidin-1-yl)pyridyl)pyrido[2,3-d]pyrimidine	2-(methoxymethyl)pyrrolidine	LRMS [M+H] ⁺ 420.

316	4-amino-5-cyclohexyl-7-(6-(N-methoxyethyl-N-propylamino)pyridyl)pyrido[2,3-d]pyrimidine	N-(methoxyethyl)propylamine	LRMS [M+H] ⁺ 421.
317	4-amino-5-cyclohexyl-7-(N-methyl-N-(2,2-dimethoxyethyl)amino)pyrido[2,3-d]pyrimidine	2-(methylamino)-dimethylacetaldehyde	LRMS [M+H] ⁺ 429.
318	4-amino-5-cyclohexyl-7-(6-(4-(dimethylamino)piperidinyl)pyridyl)pyrido[2,3-d]pyrimidine	N-(4-piperidyl)-dimethylamine	LRMS [M+H] ⁺ 433.
319	4-amino-5-cyclohexyl-7-(6-(4-(amino carbonyl)piperidinyl)pyridyl)pyrido[2,3-d]pyrimidine	piperidine-4-formamide	LRMS [M+H] ⁺ 433.

320	4-amino-5-cyclohexyl-7-(N-methyl-N-(3-(diethylamino)propyl)aminopyrid-3-yl)pyrido[2,3-d]pyrimidine	N ¹ , N ¹ -diethyl-N ¹ -methyl-1,3-propanediamine	LRMS [M+H] ⁺ 449.
321	4-amino-5-cyclohexyl-7-(6-(N-methyl-N-(4-pyridyl)ethylamino)pyrid-3-yl)pyrido[2,3-d]pyrimidine	N-methyl-(4-pyridyl)ethylamine	LRMS [M+H] ⁺ 441.
322	4-amino-5-cyclohexyl-7-(6-(N-methyl-N-(3-pyridylmethyl)amino)pyrid-3-yl)pyrido[2,3-d]pyrimidine	N-methyl-(3-pyridyl)methylamine	LRMS [M+H] ⁺ 427.

Example 323

4-amino-5-(1-(2-bromophenyl)ethyl)-7-(1-methyl-5-indolyl)pyrido[2,3-d]pyrimidine

The procedures of Example 157 were followed, except substituting 1',1'-dicyano-3-bromostyrene for the R³ reagent and 1-(1-methyl-5-indolyl)-ethanone for the R⁴ reagent. After 24 hours, the precipitated amidine compound was filtered and washed with hexanes, then dried under vacuum. The amidine compound was then heated in 1,2-dichloroethane at reflux for 1-8 hours. The reaction mixture was cooled to room temperature and purified by chromatography, and the product was recrystallized if necessary. The treatment with

aqueous HCl was omitted, and the free bases was obtained. IR (KBr) cm^{-1} 3500, 1578, 1500; MS m/z 431 (M+H)⁺.

Example 324

5 **4-amino-5-(1-(2-bromophenyl)ethyl)-7-(1-methyl-2,3-dioxo-5-indolyl)pyrido[2,3-d]pyrimidine**

The title compound was prepared from the compound of Example 323 by oxidation with CrO₃ in sulfuric acid. IR (microscope) 3471, 1765, 1500 cm^{-1} ; MS m/z 461(M+H)⁺.

10

Examples 325-326

Following the procedures of Example 157, except substituting the appropriate R³ and R⁴ reagents as indicated in the Table below, compounds of Examples 325-326 were prepared. After 24 hours, the precipitated amidine compound was filtered and washed 15 with hexanes, then dried under vacuum. The amidine compound was then heated in 1,2-dichloroethane at reflux for 1-8 hours. The reaction mixture was cooled to room temperature and purified by chromatography, and the product was recrystallized if necessary. The treatment with aqueous HCl was omitted in some cases, and the free bases were obtained.

20

Examples 325-326

Ex. No.	Name	R ³ Reagent (for 5-position)	R ⁴ Reagent (for 7-position)	Analytical Data
325	4-amino-5-(3-bromophenyl)-7-(3-fluoro-4-(1-morpholinyl)phenyl)pyrido[2,3-d]pyrimidine	1',1'-dicyano-3-bromostyrene	1-(3-fluoro-4-(1-morpholinyl)phenyl)-ethanone	IR (microscope) 3443, 3044, 1639, 1606, 1584, 1520, 1362, 1245 cm^{-1} ; MS m/z 480 (M+H) ⁺ .

326	4-amino-5-(3-bromophenyl)-7-(4-hydroxy-3-nitrophenyl)pyrido[2,3-d]pyrimidine	1',1'-dicyano-3-bromostyrene	1-(4-hydroxy-3-nitrophenyl)-ethanone	IR (KBr) 3461, 1623, 1579, 1548, 1523, 1353 cm ⁻¹ ; MS m/z 438 (M+H) ⁺ .
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Example 327

Following the procedures of Example 244 Step c, except in step c substituting the compound resulting from the reaction of 2-acetyl-5-chloropyridine in refluxing ethanol with the precursor reagent compound (4-piperidinone ethylene ketal) shown below for the R⁴ reagent of Example 244 Step c, and substituting dichloroethane as the solvent in place of the ethanol solvent in Example 244 step c, the compound shown in the table below was prepared.

10

Ex. No.	Name	precursor reagent	Analytical Data
327	4-amino-5-(3-bromophenyl)-7-(6-(4,4-ethylenedioxypiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine	4-piperidinone ethylene ketal	IR (microscope) 3091, 1602, 1580, 1558, 1512, 1353, 1236, 1103 cm ⁻¹ ; MS m/z 519 (M+H) ⁺ .

Example 328

4-amino-5-(3-bromophenyl)-7-(6-(4-oxopiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine

Treating the compound of Example 327 with dilute HCl, the title compound was prepared. IR (microscope) 3438, 3051, 1645, 1605, 1558, 1450, 1371, 1240 cm⁻¹; MS m/z 475 (M+H)⁺.

Examples 329-331

Following the procedures of Example 327, except in step c substituting the precursor reagent compound shown below for the R⁴ reagent of Example 244 Step c, and substituting dichloroethane as the solvent in place of the ethanol solvent in Example 244 step c, the compounds shown in the table below were prepared.

Examples 329-331

Ex. No.	Name	precursor reagent	Analytical Data
329	4-amino-5-(3-bromophenyl)-7-(6-(4-formylpiperazinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine	piperazine	IR (KBr) 3489, 1674, 1602, 1581, 1559, 1503, 1233, 1004 cm ⁻¹ ; MS m/z 491 (M+H) ⁺ .
330	4-amino-5-(3-bromophenyl)-7-(6-(4-methylpiperazinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine	1-methylpiperazine	IR (microscope) 3438, 3051, 1540 cm ⁻¹ ; MS m/z 477 (M+H) ⁺ .
331	4-amino-5-(3-bromophenyl)-7-(6-thiomorpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidin	thiomorpholine	IR (KBr) 3486, 1602, 1581, 1560, 1502, 1228 cm ⁻¹ ; MS m/z 479 (M+H) ⁺ .

Example 3324-amino-5-(3-bromophenyl)-7-(6-(4,4-dioxothiomorpholinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine

The compound of Example 331 was treated with 4-chloroperbenzoic acid in 5 methanol and dichloromethane to give the title compound. IR (microscope) 3471, 1601, 1581, 1562, 1510, 1353, 1316, 1285, 1122 cm⁻¹; MS m/z 511(M+H)⁺.

Example 3334-amino-5-(2-bromophenyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine

10

Step 333a. 1',1'-dicyano-2-bromostyrene

The title compound was prepared by condensation of 2-bromobenzaldehyde with malononitrile and MgO in dichloromethane by the standard procedure of Broekhuis et al. (Recl. J. R. Neth. Chem. Soc., 99: 6-12 (1980)).

15

Step 333b. 5-acetyl-2-morpholinylpyridine

The title compound was prepared by the reaction of 5-acetyl-2-chloropyridine with morpholine in refluxing ethanol.

20

Step 333c. 4-(2-bromophenyl)-3-cyano-6-morpholinylpyridine-2-amine

The title compound was prepared by condensation of 1',1'-dicyano-2-bromostyrene with 5-acetyl-2-morpholinylpyridine and ammonium acetate in dichloroethane at reflux. After the reaction was complete (TLC), the mixture was cooled, and the solvent was removed. The residue was triturated with methanol to give the product.

25

Step 333d. 4-amino-5-(2-bromophenyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine

A sample of 4-(2-bromophenyl)-3-cyano-6-morpholinylpyridine-2-amine was heated at 180-190 °C in formamide. The reaction was monitored by T.L.C. and when the 30 reaction was complete the mixture was cooled to room temperature. The product was

allowed to precipitate, then recovered by filtration and washed with water. Additional product was extracted from the filtrate. The product was purified by column chromatography eluting with 10% MeOH/CH₂Cl₂. IR (microscope) 3493, 1547, 1109cm⁻¹; MS m/z 464 (M+H)⁺.

5

Examples 334-336

Following the procedures of Example 333, except in Step a substituting the precursor aldehyde reagent shown below for the 2-bromobenzaldehyde of Example 333 Step a, and carrying the product forward as in procedures 333 Steps b-d, the compounds 10 shown in the table below were prepared.

Examples 334-336

Ex. No.	Name	precursor aldehyde reagent	Analytical Data
334	4-amino-5-(3-bromo-4-methoxyphenyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine	3-bromo-4-methoxybenzaldehyde	IR (microscope) 3486, 1600, 1575, 1562, 1500, 1260, 1237 cm ⁻¹ ; MS m/z 493 (M+H) ⁺ .
335	4-amino-5-(4-bromophenyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine	4-bromobenzaldehyde	IR (microscope) 3497, 1532, 1098cm ⁻¹ ; MS m/z 464 (M+H) ⁺ .

336	4-amino-5-(3-chlorophenyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine	3-chlorobenzaldehyde	IR (microscope) 3484, 1500, 1034cm ⁻¹ ; MS (FAB) m/z 587 (M+H) ⁺ .
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Example 3374-amino-5-(3-bromophenyl)-7-(5-chloro-6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine

5 Following the procedures of Example 333, except in Step a substituting 3-bromobenzaldehyde for the 2-bromobenzaldehyde, in Step b substituting 5-acetyl-2,3-dichloropyridine for the 5-acetyl-2-chloropyridine to give 5-acetyl-3-chloro-2-morpholinylpyridine, and substituting 5-acetyl-3-chloro-2-morpholinylpyridine for the 5-acetyl-2-morpholinylpyridine in step c, then the carrying the product forward as in

10 Example 333 Step d, the title compound was prepared. IR (microscope) 3493, 1635, 1585, 1555, 1492, 1340, 1241, 1113 cm⁻¹; MS m/z 497 (M+H)⁺.

Example 3384-amino-5-(3-bromophenyl)-7-(6-(N-oxidomorpholinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine

15 The title compound was prepared by treating the compound of Example 134 with hydrogen peroxide in acetic acid according to standard procedures. IR (microscope) 3486, 1579, 1552, 1353, 1121, 1020 cm⁻¹; MS m/z 479 (M+H)⁺.

Example 3394-amino-5-(3-bromophenyl)-7-(6-(N-(2-hydroxyethoxyethyl)amino)-3-pyridyl)pyrido[2,3-d]pyrimidine5 Step 339a. 1',1'-dicyano-3-bromostyrene

The title compound was prepared by condensation of 3-bromobenzaldehyde with malononitrile and MgO in dichloromethane by the standard procedure of Broekhuis et al. (Recl. J. R. Neth. Chem. Soc., 99: 6-12 (1980)).

10 Step 339b. 5-acetyl-2-(N-(2-ethoxyethyl)amino)pyridine

The title compound was prepared by the reaction of 5-acetyl-2-chloropyridine with 2-ethoxyethylamine in refluxing ethanol.

Step 339c. 4-(3-bromophenyl)-3-cyano-6-(N-(2-ethoxyethyl)amino)pyridine-2-amine

15 The title compound was prepared by condensation of 1',1'-dicyano-2-bromostyrene with 5-acetyl-2-morpholinylpyridine and ammonium acetate in dichloroethane at reflux. After the reaction was complete (TLC), the mixture was cooled, and the solvent was removed. The residue was triturated with methanol to give the product.

20 Step 339d. 4-amino-5-(2-bromophenyl)-7-(6-(N-(2-ethoxyethyl)amino)-3-pyridyl)pyrido[2,3-d]pyrimidine

A sample of the compound from Step 239d was treated according to the procedure of Example 233d to give the title compound. IR (microscope) 3301, 1610, 1579, 1543, 1346, 1304, 1120 cm^{-1} ; MS m/z 481 ($\text{M}+\text{H}$) $^{+}$.

Example 3404-amino-5-(3-bromophenyl)-7-(6-(N-(2-hydroxyethoxyethyl)-N-formylamino)-3-pyridyl)pyrido[2,3-d]pyrimidine

This compound was isolated by chromatography as a product of the reaction
5 described in Example 239 Step d. IR (microscope) 3306, 1679, 1596, 1577, 1548, 1493, 1352, 1125 cm⁻¹; MS m/z 509 (M+H)⁺.

Example 3414-amino-5-(3-bromophenyl)-7-(6-(N-(2-hydroxyethoxyethyl)-3-pyridyl-N-oxide)pyrido[2,3-d]pyrimidine

10 The title compound was prepared by treating the compound of Example 341 with hydrogen peroxide in acetic acid according to standard procedures. IR (microscope) 3296, 1628, 1560, 1411, 1353 cm⁻¹; MS m/z 497 (M+H)⁺.

Example 3424-amino-5-(3-bromophenyl)-7-(6-(4-hydroxypiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine

15 The title compound was prepared from the compound of Example 328 by reduction with (Lithium Aluminum Hydride, and subsequent workup according to 20 standard procedures). IR (microscope) 3349, 1510, 1116 cm⁻¹; MS m/z 478 (M+H)⁺.

Example 3431-(5-(4-amino-5-(3-bromophenyl)pyrido[2,3-d]pyrimidin-7-yl)-2-pyridyl)-piperidine-4-phosphate, disodium salt

25 The title compound was prepared from the compound of Example 342 by treatment with POCl₃, and subsequent workup according to standard procedures. IR (microscope) 3498, 1500, 1444 cm⁻¹; MS m/z 556 (M+H)⁺.

Example 3444-amino-5-(3-bromophenyl)-7-(6-(2-hydroxy)morpholiny)-3-pyridyl)pyrido[2,3-d]pyrimidine

The title compound was prepared from the compound of Example 339 by 5 oxidation of the free hydroxy group to an aldehyde with TEMPO reagent. During workup of the mixture, the compound self-condensed to give the title compound. MS m/z 492 (M+CH₃OH-H₂O)⁺.

Example 34510 4-amino-5-(3-bromophenyl)-7-(4-methylene)piperidiny)-3-pyridyl)pyrido[2,3-d]pyrimidine

The title compound was prepared from the compound of Example 328 by 15 treatment with methyl triphenylphosphine bromide at -78 °C in DMSO. After quenching and warming the mixture to room temperature, the title compound was extracted, then purified by chromatography. IR (microscope) 3055, 1602, 1559, 1508, 1440, 1344, 1174 cm⁻¹; MS m/z 473 (M+H)⁺.

Example 34620 4-amino-5-(3-bromophenyl)-7-(4-hydroxy-4-(hydroxymethyl)piperidiny)-3-pyridyl)pyrido[2,3-d]pyrimidine

The title compound was prepared from the compound of Example 345 by 25 treatment with OsO₄ in DMSO at room temperature. After quenching, the title compound was extracted, then purified by chromatography. IR (microscope) 3304, 1603, 1580, 1557, 1509, 1352, 1241 cm⁻¹; MS m/z 507 (M+H)⁺.

Example 3474-amino-5-(cyclohexyl)-7-(6-(4,4-ethylenedioxypiperidiny)-3-pyridyl)pyrido[2,3-d]pyrimidine30 Step 347a. 1,1-dicyano-3-cyclohexylethene

The 1,1-dicyano-3-cyclohexylethene was prepared according to the method of Moison, et al. (Tetrahedron (1987), 43:537-542) by treating cyclohexane carboxaldehyde with malononitrile in the presence of finely powdered magnesium oxide in dichloromethane.

5

Step 347b. 2-acetyl-5-(4,4-ethylenedioxypiperidinyl)pyridine

A sample of 2-acetyl-5-chloropyridine was treated in refluxing ethanol with 4-piperidinone ethylene ketal to give the title compound.

10 Step 347c. 4-amino-5-cyclohexyl-7-(6-(4,4-ethylenedioxypiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine

Following the procedures of example 339 Step c, except substituting the compounds from Step 347a and 347b for the compounds of Steps 339a and 339b, and carrying the product forward according to the procedure of example 339 Step d, the title 15 compound was prepared. IR (microscope) 2929, 1604, 1585, 1557, 1514, 1426, 1344, 1238, 1106 cm⁻¹; MS m/z 447 (M+H)⁺.

Example 348

4-amino-5-cyclohexyl-7-(6-(4-oxo-piperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine

20 The title compound was prepared from the compound of Example 347 by treatment with dilute HCl in ethanol. The title compound was purified by chromatography. IR (microscope) 2928, 1715, 1603, 1585, 1559, 1507, 1344, 1226 cm⁻¹; MS m/z 403 (M+H)⁺.

25

Example 349

4-amino-5-cyclohexyl-7-(6-(4-methylenepiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine

The title compound was prepared from the compound of Example 348 by treatment with methyl triphenylphosphine bromide at -78 °C in DMSO. After quenching and warming the mixture to room temperature, the title compound was extracted, then

purified by chromatography. IR (microscope) 2929, 1604, 1584, 1557, 1506, 1342, 1239 cm⁻¹; MS m/z 401 (M+H)⁺.

Example 350

5 4-N-(iminomethyl)amino-5-cyclohexyl-7-(6-dimethylamino-3-pyridyl)pyrido[2,3-d]pyrimidine

This compound was isolated from the reaction mixture of Example 293 as a side product: IR (cm-1) 3289, 3089, 2930, 2841, 1674, 1606, 1559, 1531. LRMS [M+H]⁺ m/z 376.

10

Example 351

(S)-4-amino-S-(3-bromophenyl)-7-(6-(O-methyl-2-hydroxymethyl)pyrrolidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine

Prepared as described for Examples 2-156; using (S)-1-(6-(O-methyl-2-pyrrolidinemethanol)-3-pyridinyl)ethanone as R₁ reagent (for position 7) and 3-bromobenzaldehyde for R₃ reagent (for 5-position).
MS (ESI(+)) 489/491 (M+H⁺; ⁷⁹Br/⁸¹Br);
IR (KBr pellet) ν_{max} 3484, 3203, 1603, 1581, 1556 cm⁻¹.

20

Example 352

(S)-4-amino-5-(3-bromophenyl)-7-(6-(2-hydroxy ethyl)pyrrolidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine

Prepared as described for Examples 2-156; using (S)-1-(6-(2-pyrrolidinemethanol)-3-pyridinyl)ethanone as R₁ reagent (for position 7) and 3-bromobenzaldehyde for R₃ reagent (for 5-position).
MS (ESI(+)) 477/479 (M+H⁺; ⁷⁹Br/⁸¹Br);
IR (KBr pellet) ν_{max} 3487, 3303, 3208, 2949, 1605, 1577, 1558, 1510, 1415, 1351, 1244, 1158, 828, 704 cm⁻¹.

30

Example 353

4-amino-5-(2-bromophenyl)-7-(6-(4-hydroxypiperidinyl)-3-pyridinyl)pyrido[2,3-d]pyrimidine

Prepared as described for Examples 2-156, using 1-(6-(4-hydroxypiperidine)-3-pyridinyl)ethanone as R₄ reagent (for position 7) and 2-bromobenzaldehyde for R₃ reagent (for 5-position).

MS (ESI(+)) 477/479 (M+H⁺; ⁷⁹Br/⁸¹Br);

IR (KBr pellet) ν_{max} 3485, 3298, 3198, 2938, 2848, 1600, 1574, 1557, 1351, 1225, 1024, 766 cm⁻¹.

10 Example 354

4-amino-5-(4-fluorophenyl)-7-(6-(4,4-ethylenedioxypiperidinyl)-3-pyridinyl)pyrido[2,3-d]pyrimidine

Prepared as described for Example 327: using 4-fluorobenzaldehyde instead of 3-bromobenzaldehyde as precursor reagent as described in example 244 Step C.

15 MS (ESI(+)) 459 (M+H)⁺;

IR (KBr pellet) ν_{max} 3487, 3299, 3066, 1959, 1604, 1577, 1559, 1510, 1355, 1235, 1107, 943, 897, 792 cm⁻¹.

Example 355

20 4-amino-5-(2-bromophenyl)-7-(6-(4-hydroxypiperidinyl)-3-pyridazyl)pyrido[2,3-d]pyrimidine

Prepared as described for Examples 301-305, using 4-hydroxypiperidine as reagent for Step C (to prepare correct R₄ reagent).

MS (ESI(+)) 478/480 (M+H⁺; ⁷⁹Br/⁸¹Br);

25 IR (KBr pellet) ν_{max} 3487, 3312, 1576, 1549, 1486, 1353, 1081 cm⁻¹.

Example 356

4-amino-5-(3-bromophenyl)-7-(6-(4,4-ethylenedioxypiperidinyl)-3-pyridazyl)pyrido[2,3-d]pyrimidine

30 Prepared as described for Examples 301-305; using 4-piperidinone ethylene ketal

as reagent for Step C (to prepare correct R₁ reagent).

MS (ESI(+)) 520/522 (M+H⁺; ⁷⁹Br⁸¹Br);

IR (KBr pellet) ν_{max} 3476, 3297, 1574, 1561, 1461, 1354, 1145, 1103 cm⁻¹.

5

Example 357

4-amino-5-(3-bromophenyl)-7-(2-morpholinyl-5-thiazovl)pyrido[2,3-d]pyrimidine

A solution of the product from 357d (2.49 g, 5.30 mmol) in o-dichlorobenzene (15 mL) was heated to reflux overnight. The reaction mixture was cooled to room temperature, the solid collected by filtration and purified by silica gel chromatography 10 (elution with 3% methanol:dichloromethane) to provide 1.06 g (43%) of the desired title product as a yellow solid. mp: >280 °C; MS (DCI/NH₃) m/z 469/471 (M+H)⁺; IR (microscope) 3481, 2046, 1506, 1491, 1116 cm⁻¹.

357a: 2-morpholinylthiazole

15 2-bromothiazole (12.63 g, 77.00 mmol) in morpholine (30.0 mL) was sealed into a tube and heated to 100 °C for 3 days. The mixture was cooled, partitioned between water and dichloromethane, the layers separated and the organic phase dried (Na₂SO₄) and concentrated to afford 12.5 g (95%) of the desired compound as a brown oil. Material used directly in the next reaction. MS (DCI/NH₃) m/z 171 (M+H)⁺.

20

357b: 5-acetyl-2-morpholinylthiazole

A solution of the product from Example 357a (7.20 g, 42.3 mmol) in tetrahydrofuran (80 mL) at -78 °C was treated with N-BuLi (2 M in hexanes, 23.5 mL). After 30 minutes, the reaction mixture was transferred via cannula to a solution of acetic 25 anhydride (10 mL) in tetrahydrofuran (50 mL) at -60 °C and stirred for 1 hour. The slurry was then warmed to room temperature for an additional 30 minutes, quenched with saturated sodium bicarbonate and extracted with diethyl ether. The organic phase was dried (Na₂SO₄), concentrated and purified by silica gel chromatography (elution with 50% dichloromethane/ethyl acetate) to provide 3.70 g (41%) of the desired compound. MS 30 (DCI/NH₃) m/z 213 (M+H)⁺.

357c: 4-(3-Bromophenyl)-3-cyano-6-(2-morpholinethiazolo)pyridine-2-amine

10 A slurry of the product from 357b (4.91 g, 23.1 mmol) and ammonium acetate (9.75 g, 127 mmol) in 1,2-dichloroethane (50 mL) was treated with 2-(3-bromobenzylidene)malononitrile (10.78 g, 46.3 mmol; J. Am. Chem. Soc. 1949, 71, 2949) and the mixture heated to reflux overnight. The solution was cooled to room temperature, hexanes (50 mL) added and stirring continued for 3 hours. The solid was collected by filtration, washed with methanol and dried to provide 4.57 g (45%) of the desired material as an orange solid. MS (DCI/NH₃) m/z 442/444 (M+H)⁺.

10

357d: 4-(3-Bromophenyl)-3-cyano-6-(2-morpholinethiazolo)pyridine-2-amidine

15 A solution of the product from 357c (1.50 g, 3.39 mmol) and triethylorthoformate (34 mL) with a catalytic amount of ammonium sulfate was heated to reflux for 6 hours. The dark mixture was cooled, ammonia in ethanol (2 M, 70 mL) added and the mixture stirred overnight. The solid product was collected by filtration and dried to provide 1.17 g (73%) of the desired product as a yellow solid. MS (DCI/NH₃) m/z 469/471 (M+H)⁺.

Example 358

20 4-amino-5-(N-methyl-3-indolyl)-7-(6-morpholinyl-3-pyridinyl)pyrido[2,3-d]pyrimidine
Prepared as described for Examples 2-156; using 1-(6-morpholinyl-3-pyridinyl)ethanone as R₁ reagent (for position 7) and N-methylindole-3-carboxaldehyde for R₃ reagent (for 5-position).
MS (DCI/NH₃) 438 (M+H)⁺;
IR (mic) 3453, 1641, 1556, 1244, 1120 cm⁻¹.

25

Example 359

25 4-amino-5-(3-bromophenyl)-7-(6-(4-ethoxyiminopiperidinyl)-3-pyridinyl)pyrido[2,3-d]pyrimidine
A suspension of Example 328 (282 mg, 0.593 mmol) in absolute ethanol (3 mL) 30 was treated sequentially with ethoxyamine hydrochloride (64 mg, 0.65 mmol), and 2 drops

conc. aq. HCl, heated to reflux 1.5 hours, cooled and partitioned, between CH₂Cl₂ (25 mL) and saturated NaHCO₃ (15 mL). The separated aqueous phase was extracted with CH₂Cl₂ (1 x 10 mL), and the combined organic layers were washed with brine, dried (Na₂SO₄), and concentrated in vacuo. The crude product was purified by flash chromatography

5 eluting with 5% MeOH/CH₂Cl₂ to yield 240 mg (78%) of the designated compound.

¹H NMR (300 MHz, DMSO-d₆) δ 1.19 (t, 3H), 2.41 (m, 2H), 2.58 (m, 2H), 3.77-3.86 (m, 4H), 4.02 (q, 2H), 6.99 (d, 1H), 7.50-7.60 (m, 2H), 7.79 (dt, 1H), 7.85 (m, 2H), 8.47 (dd, 1H), 8.53 (s, 1H), 9.08 (d, 1H);

MS (DCI/NH₃) m/e 518/520 (M+H)⁺;

10 Anal. calcd for C₂₅H₂₄BrN₂O: C, 57.92; H, 4.67; N, 18.91. Found: C, 57.69; H, 4.66; N, 18.65.

Example 360

4-amino-5-(3-bromophenyl)-7-(6-(4-ethylcarbomethoxyiminopiperidinyl)-3-pyridinyl)pyrido[2,3-d]pyrimidine

Prepared as described for Example 359, substituting carbomethoxylamine for ethoxyamine.

¹H NMR (300 MHz, DMSO-d₆) δ 1.20 (t, 3H), 2.42 (m, 2H), 2.65 (m, 2H), 3.77-3.90 (m, 4H), 4.13 (q, 2H), 4.61 (s, 2H), 7.01 (d, 1H), 7.55 (m, 2H), 7.79 (dt, 1H), 7.86 (m, 2H), 8.48 (dd, 1H), 8.53 (s, 1H), 9.09 (d, 1H); MS (DCI/NH₃) m/e 576/578 (M+H)⁺;

20 Anal. calcd for C₂₁H₂₆BrN₂O-0.5 H₂O: C, 55.39; H, 4.65; N, 16.75. Found: C, 55.66; H, 4.61; N, 16.37.

Example 361

4-(N-(2,3-dihydroxypropyl)amino)-5-(3-bromophenyl)-7-(6-morpholinyl-3-pyridinyl)pyrido[2,3-d]pyrimidine

Example 134 formamide complex (200 mg, 0.339 mmol) and 3-amino-1,2-propanediol (155 mL, 2.0 mmol) were placed in a 50 mL round-bottomed flask furnished with a magnetic stirbar. DMSO (dimethyl sulfoxide) (6 mL) was added. The mixture was

30 then heated to 120 °C for about 10 min until a homogeneous solution was formed.

Catalytic amount of acetic acid was then added, and the reaction mixture was allowed to stir at 120 °C for about 1.5 days. DMSO was removed under vacuum. The residue was dissolved in CH₂Cl₂, and washed with water, NaHCO₃ (saturated), water, and then dried over Na₂SO₄. The crude mixture was first purified by column chromatography (SiO₂), 10% 5 MeOH/CH₂Cl₂). The desired product was collected and was subjected to another column chromatographic purification (SiO₂, ethyl acetate and then 25% NCCH₃, 7.5% MeOH and 67.5% CH₂Cl₂) to give a pure yellow solid (60 mg, 29% yield; M.P. 189-191 °C).
 MS (ESI(+)) = 537/539 (M+H⁺); ⁷⁹Br/⁸¹Br;
 IR (MIC) ν_{max} = 3433, 3354, 2914, 2853, 1568, 1506, 1236, 1114, 945 cm⁻¹.

10

Example 362

4-(N-(3-morpholinylpropyl)amino)-5-(3-bromophenyl)-7-(6-morpholinyl-3-pyridinyl)pyrido[2,3-d]pyrimidine

Prepared as described for Example 360, but replacing 3-amino-1,2-propanediol 15 with 4-(3-aminopropyl)morpholine.
 MS (ESI(+)) = 590/592 (M+H⁺); ⁷⁹Br/⁸¹Br;
 IR (MIC): ν_{max} = 3433, 2959, 2854, 1567, 1506, 1235, 1117, 945 cm⁻¹.

20

Example 363

4-(N-(2-(4-imidazolyl)ethyl)amino)-5-(3-bromophenyl)-7-(6-morpholinyl-3-pyridinyl)pyrido[2,3-d]pyrimidine

Prepared as described for Example 360, but replacing 3-amino-1,2-propanediol with histamine.
 MS (ESI(+)) = 557/559 (M+H⁺); ⁷⁹Br/⁸¹Br;
 25 IR (MIC) ν_{max} = 3433, 3091, 2954, 2893, 2854, 1571, 1564, 1505, 1235, 1123, 944 cm⁻¹.

Example 364

4-(N-(3-carboxypropyl)amino)-5-(3-bromophenyl)-7-(6-morpholinyl-3-pyridinyl)pyrido[2,3-d]pyrimidine

Prepared as described for Example 360, but replacing 3-amino-1,2-propanediol with 3-aminopropionic acid (β -alanine).

MS (ESI(+)) = 53 5/537 (M+H $^+$; $^{79}\text{Br}^{81}\text{Br}$);

IR (MIC) ν_{max} = 3429, 3051, 2959, 2855, 2528, 1927, 1718, 1585, 1559, 1352, 1332, 1236,

5 1118, 944 cm^{-1} .

Example 365

4-amino-5-(3-bromophenyl)-7-(6-(4-oxopiperidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine

10 Prepared as described for Example 328; substituting Example 356 for Example 327.

MS (APCI+) m/z 475 (M+H) $^+$;

^1H NMR (300 MHz, DMSO-d₆) δ 8.60(s, 1H), 8.45(d, 1H), 8.28(s, 1H), 7.85 (m, 2H), 7.50 (m, 3H), 4.10 (m, 4H).

15 Example 366

4-amino-5-(3-bromophenyl)-7-(6-(4-morpholinyliminopiperidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine

Prepared as described for Example 359; substituting Example 365 for Example 328 and 4-aminomorpholine for ethoxylamine hydrochloride.

20 MS (APCI+) m/z 560 (M+H) $^+$;

^1H NMR (300 MHz, DMSO-d₆) δ 8.59(s, 1H), 8.40(d, 1H), 8.26(s, 1H), 7.84 (m, 2H), 7.55 (m, 3H), 3.93 (m, 4H), 3.68 (m 4H), 2.75 (m, 2H), 2.63 (m, 4H), 2.47 (m, 2H)

Example 367

25 4-amino-5-(3-bromophenyl)-7-(6-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptan-5-yl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine

stepa 4-amino-5-(3-bromo phenyl)-7-(6-chloro-3-pyridazinyl) pyrido[2,3-d]pyrimidine

Prepared by a modification of the method of Example 333 step C, a mixture of 22

mmol of 3-acetyl-6-chloropyridazine (Example 246), 26 mmol of 1-(3-bromophenyl) 1,1-

30 dicyanoethylene, and 110 mmol of ammonium acetate in 150 mL of dichloroethane was

heated at reflux for an hour to give the intermediate amino cyanopyridine, which was purified by flash column chromatography. By a modification of the method of Example 287, the intermediate 2-amino-3-cyano-4-(3-bromo phenyl)-6-((6-chloro) pyridazin-3-yl)pyridine was heated in 40 mL of triethylorthoformate with 1 mmol of ammonium sulfate for one hour. A 2M solution of ammonia in ethanol was added (30 mL) stirring, and after 14 hours, the solid amidine intermediate was collected by filtration and dried in vacuo. The amidine intermediate was then heated in 25 mL of 1,2-dichlorobenzene at 120 °C for two hours. On cooling, a precipitate was deposited. Ether was added, and the precipitate was collected by filtration, washed with ether and dried.

10 M/z [M+H]⁺ C₁₇H₁₀N₆BrCl at 413,414,415.
¹H NMR (CD₃CO₂D) δ 8.72 (d, J = 8.7 Hz, 1 H), 8.64 (s, 1 H), 8.48 (s, 1 H), 7.73 (d, J = 8.7 Hz, 1 H), 7.70 (t, J = 1.0 Hz, 1 H), 7.64 (dt, J = 8.1, 1.0 Hz), 7.45 (dt, J = 8.1, 1.0 Hz, 1 H), 7.42 (m, 1H).

15 4-amino-5-(3-bromophenyl)-7-(6-(1S,4S)-2-aza-5-oxa-bicyclo[2.2.1]heptane)-3-pyridazinyl)pyrido[2,3-d]pyrimidine
A solution of 0.73 mmol of 4-amino-5-(3'-bromo phenyl)-7-(6-(chloro) pyridazin-3-yl) [2,3-d] pyridopyrimidine (prepared in step a), 3.1 mmol of (1S,4S)-2-aza-5-oxa-bicyclo[2.2.1]heptane (Aldrich Chemical Co.), and 2.4 mmol of potassium carbonate was heated at 120 °C in DMSO for 14 hours, then cooled and poured into 10 mL of water. The mixture was partitioned between dichloromethane and water, and the organic phase was dried (Na₂SO₄), and concentrated in vacuo to give the title compound. This material was recrystallized from chloroform/methanol and converted to the hydrochloride salt by lyophilization from 12 mL of 2.5 M HCl.

20 mp 222-226 °C;
CHN calculated for C₂₂H₁₈N₆OBr(3.0 HCl): C 45.11, H 3.61, N 16.74; found: C 45.00, H 3.90, N 16.82. MS [M+H]⁺ at 478;
IR 3434, 3056, 1640, 1610, 1558, 1376 cm⁻¹.

4-amino-5-(3-bromophenyl)-7-(6-(4-methoxyminopiperidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine

Prepared as described for Example 359 substituting Example 365 for Example 328 and methoxylamine hydrochloride for ethoxylamine hydrochloride.

5 MS (ESI+) m/z 504 (M+H)⁺;

¹H NMR (300 MHz, DMSO-d₆) δ 8.59 (s, 1H), 8.40 (d, 1H), 8.26 (s, 1H), 7.82 (m, 2H), 7.54 (m, 3H), 3.90 (m, 4H), 3.77 (s, 1H), 2.62 (m, 2H), 2.47 (m, 2H)

Example 369

10 4-amino-5-(3-bromophenyl)-7-(6-phenylmethoxy-3-pyridazinyl)pyrido[2,3-d]pyrimidine

Sodium and benzyl alcohol were heated at 60 °C in toluene for 3 hours. It was cooled to room temperature and added to a suspension of 4-amino-5-(3-bromo phenyl)-7-(6-chloro-3-pyridazinyl) pyrido[2,3-d]pyrimidine (prepared in Example 367) in anhydrous DMSO to give the title compound. Treatment with 1M HCl ether in chloroform and

15 methanol at room temperature provided the HCl salt.

MS (ESI+) m/z 485 (M+H)⁺;

¹H NMR (300 MHz, DMSO-d₆) δ 10.07 (bs, 1H), 8.95 (s, 1H), 8.59 (d, 1H), 8.50 (s, 1H), 7.95-7.30 (m, 10H), 5.63 (s, 2H)

Example 370

20 4-amino-5-(3-bromophenyl)-7-(6-(4-methoxypiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine

Step a 2-amino-3-cyano-4-(3-bromophenyl)-6-(6-chloro-3-piridyl)pyridine

Prepared as described in Example 244 substituting 5-acetyl-2-chloropyridine for 5-acetyl-1-methylindoline in step c.

25

Step b 4-amino-5-(3-bromophenyl)-7-(6-chloro-3-pyridyl)pyrido[2,3-d]pyrimidine

2-Amino-3-cyano-4-(3-bromophenyl)-6-(6-chloro-3-piridyl)pyridine prepared in step a was reacted with 10 eq. of N,N',N"-methylidynetriformamide in formamide at 125° for 3 days. The slurry was cooled, poured into 3 volumes of water, and the resulting solid

was collected by filtration and washed with water. The chloropyridyl product was dried under vacuum and used without further purification.

step c 4-methoxypiperidine

5 4-Hydroxypiperidine is treated with 1 eq. of Boc_2O in CH_2Cl_2 and stirred at room temperature for 5 min. The solution is then washed with water and brine, dried over Na_2SO_4 , and concentrated in vacuo. The protected species is then dissolved in DMF and treated with 7 eq. of NaH. The mixture is stirred for 5 min. then methyl iodide (2 eq) is added, and the reaction is stirred at room temperature overnight. After this time, it is 10 quenched with water and extracted with 2:1 ether-hexanes. The organic solution is dried (Na_2SO_4) and concentrated in vacuo. The oil thus obtained is finally stirred in 4M HCl-dioxane for 30 minutes. The solvent was removed in vacuo, then the residue was basified with 50% aq. NaOH solution and extracted with ether. Drying (Na_2SO_4) of the extracts, followed by removal of the solvent in vacuo, afforded 4-methoxypiperidine.

15

Step d.

20 3.0 equivalents of 4-methoxypiperidine (step c) and 1 equivalent of 4-amino-5-(3-bromophenyl)-7-(6-chloro-3-pyridyl)pyrido[2,3-d]pyrimidine (step b) were stirred in DMSO at 100° for 16 hours. The mixture was cooled, quenched with 3 volumes of water, and the precipitated solid was collected by filtration and washed with water. Purification by recrystallization afforded the title compound. ^1H NMR (300 MHz, $\text{d}_6\text{-DMSO}$) δ 9.05 (d, 1H), 8.52 (s, 1H), 8.42 (dd, 1H), 7.84 (d, 1H), 7.83 (s, 1H), 7.78 (dt, 1H), 7.54 (2 overlapping m, 2H), 6.99 (br d, 1H), 4.07 (m, 2H), 3.45 (m, 2H), 3.36 (m, 1H), 3.29 (s, 3H), 1.92 (m, 2H), 1.46 (m, 2H); MS (ESI) m/z 491/493 ($\text{M}^+ + \text{H}$, $^{79}\text{Br}/^{81}\text{Br}$).

25

Example 371

4-amino-5-(3-bromophenyl)-7-(6-(4-(4-tetrahydropyranloxy)iminopiperidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine

Prepared as described for Example 359; substituting Example 365 for Example 328 and O-tetrahydro-2H-pyran-4-yl-hydroxylamine hydrochloride (JP 94-177353 19940729) for ethoxylamine hydrochloride.

MS (ESI+) m/z 574 (M+H)⁺;

5 ¹H NMR (300 MHz, CDCl₃-d1) δ 8.78 (s, 1H), 8.69 (d, 1H), 8.59 (s, 1H), 7.71 (m, 2H), 7.46 (m, 2H), 7.10 (d, 1H), 4.26 (m, 1H), 3.98 (m, 6H), 3.53 (m, 2H), 2.79 (m, 2H), 2.59 (m, 2H), 2.00 (m, 2H), 1.69 (m, 2H)

Example 372

10 4-amino-5-(3-bromophenyl)-7-(6-isobutoxy-3-pyridazinyl)pyrido[2,3-d]pyrimidine

Sodium isobutoxide was made by heating sodium and isobutanol at 60°C for 45 minutes. 4-amino-5-(3-bromo phenyl)-7-(6-chloro-3-pyridazinyl) pyrido[2,3-d]pyrimidine (prepared as in Example 367) was added to this mixture and heated at 60°C for 2 hours to give the title compound.

15 MS (APCI+) m/z 451 (M+H)⁺;

¹H NMR (300 MHz, DMSO-d₆) δ 10.07 (bs, 1H), 8.96 (s, 1H), 8.53 (s, 1H), 8.52 (d, 1H), 7.95 (m, 1H), 7.85 (m, 1H), 7.60 (m, 3H), 4.34 (d, 2H), 2.15 (m, 1H), 1.05 (d, 6H)

Example 373

20 4-amino-5-(3-bromophenyl)-7-(6-(4-(N-methylpiperazinyl)iminopiperidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine

Prepared as described for Example 359; substituting Example 365 for Example 328 and 4-amino-4-N-methylpiperazine for ethoxylamine hydrochloride.

MS (APCI+) m/z 575 (M+H)⁺;

25 ¹H NMR (300 MHz, DMSO-d₆) δ 8.59 (s, 1H), 8.42 (d, 1H), 8.27 (s, 1H), 7.84 (m, 2H), 7.55 (m, 3H), 3.92 (m, 4H), 2.71 (m, 4H), 2.63 (m, 4H), 2.43 (m, 4H), 2.19 (s, 3H)

Example 374

30 4-amino-5-(3-bromophenyl)-7-(6-(4-tetrahydropyranloxy)-3-pyridazinyl)pyrido[2,3-d]pyrimidine

Prepared as described for Example 369; substituting tetrahydro-4H-pyran-4-ol for benzyl alcohol.

MS (FAB+) m/z 479 (M+H)⁺;

¹H NMR (300 MHz, DMSO-d₆) δ 9.80 (bs, 1H), 8.85 (s, 1H), 8.56 (d, 1H), 8.52 (s, 1H),

5 7.93 (m, 1H), 7.84 (m, 1H), 7.70-7.50 (m, 3H), 5.51 (m, 1H), 3.91 (m, 2H), 3.55 (m, 2H),
2.13 (m, 2H), 1.77 (m, 2H)

Example 375

4-amino-5-(3-bromophenyl)-7-(6-morpholinylethoxy-3-pyridazinyl)pyrido[2,3-

10 d]pyrimidine

Prepared as described for Example 369; substituting N-(2'-hydroxylethyl)-morpholine for benzyl alcohol.

MS (FAB+) m/z 508 (M+H)⁺;

¹H NMR (300 MHz, DMSO-d₆) δ 12.10 (bs, 1H), 10.05 (bs, 1H), 8.92 (s, 1H), 8.57 (d,

15 1H), 8.48 (s, 1H), 7.95-7.52 (m, 5H), 7.45 (bs, 2H), 5.05 (m, 2H), 3.97 (m, 4H), 3.69 (m,
2H), 3.60-3.18 (m, 4H)

Example 376

4-amino-5-(3-bromophenyl)-7-(6-(4-ethoxypiperidinyl)-3-pyridazinyl)pyrido[2,3-

20 d]pyrimidine

Treatment of N-Boc-4-hydroxylpiperidine with sodium hydride and ethyl iodide gave N-Boc-4-ethoxypiperidine, which was treated with 4M HCl in dioxane to give 4-ethoxypiperidine.

25 The title compound was prepared as described for Example 367 substituting 4-ethoxypiperidine for (1S,4S)-2-aza-5-oxa-bicyclo[2.2.1]heptane, followed by treatment with 1M HCl ether.

MS (FAB+) m/z 506 (M+H)⁺;

¹H NMR (300 MHz, DMSO-d₆) δ 10.10 (bs, 1H), 8.90 (s, 1H), 8.38 (s, 1H), 8.26 (d, 1H),
7.92-7.42 (m, 5H), 3.78-3.38 (m, 7H), 1.96 (m, 2H), 1.55 (m, 2H), 1.10 (t, 3H)

30

Example 3774-amino-5-(3-bromophenyl)-7-(6-(4-(2-ethoxyethoxy)piperidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine

Treatment of N-Boc-4-hydroxylpiperidine with sodium hydride and chloroethyl
5 ethyl ether gave N-Boc-4-(2'-ethoxy-ethoxy)-piperidine, which was treated with 4M HCl
in dioxane to give 4-(2'-ethoxy-ethoxy)-piperidine.

The title compound was prepared as described for Example 367 substituting 4-(2'-ethoxy-ethoxy)-piperidine for (1S,4S)-2-aza-5-oxa-bicyclo[2.2.1]heptane, followed by treatment with 1M HCl ether.

10 MS (APCI+) m/z 550 (M+H)⁺;
¹H NMR (300 MHz, DMSO-d₆) δ 10.10 (bs, 1H), 8.94 (s, 1H), 8.41 (s, 1H), 8.23 (d, 1H),
7.95-7.45 (m, 5H), 7.39 (bs, 1H), 4.15 (m, 3H), 3.70-3.30 (m, 6H), 1.94 (m, 3H), 1.50 (m,
3H), 1.08 (t, 3H)

15 Example 378

4-amino-5-(3-bromophenyl)-7-(6-(4-(4-tetrahydropyranloxyethyl)piperidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine

4-(2'-Hydroxylethyl)-piperidine was treated with triethylamine and Boc-anhydride
in THF at room temperature. This crude product was treated with mesyl chloride and
20 triethylamine in dichloromethane to give the mesylate. This mesylate was then treated
with sodium tetrahydro-4H-pyran-4-oxide (Example 372), followed by deprotection with
4M HCl in dioxane to give 4-(2'-(4"-azacyclohexyl)-ethoxy)-tetrahydro-4H-pyran.

The title compound was prepared as described for Example 367 substituting 4-(2'-
(4"-azacyclohexyl)-ethoxy)-tetrahydro-4H-pyran for (1S,4S)-2-aza-5-oxa-
25 bicyclo[2.2.1]heptane, followed by treatment with 1M HCl ether.

MS (APCI+) m/z 590 (M+H)⁺;

¹H NMR (300 MHz, DMSO-d₆) δ 10.10 (bs, 1H), 8.79 (s, 1H), 8.22 (s, 1H), 8.18 (d, 1H),
7.70-7.40 (m, 5H), 4.42 (m, 2H), 3.63 (m, 2H), 3.34 (m, 3H), 3.19 (m, 2H), 3.01 (m, 2H),
1.70 (m, 5H), 1.33 (m, 2H), 1.23 (m, 2H), 1.08 (m, 2H)

30

Example 3794-amino-5-(3-bromophenyl)-7-(6-(3-(R)-tetrahydrofuranyloxy)piperidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine

Prepared as described for Example 369; substituting (R)-3-hydroxytetrahydrofuran for benzyl alcohol.

MS (APCI+) m/z 465 (M+H)⁺;
¹H NMR (300 MHz, DMSO-d₆) δ 10.08 (bs, 1H), 8.93 (s, 1H), 8.52 (d, 1H), 8.51 (s, 1H), 7.98-7.40 (m, 6H), 5.80 (m, 1H), 4.05-3.78 (m, 4H), 2.36 (m, 1H), 2.15 (m, 1H)

10 Example 3804-amino-5-(3-bromophenyl)-7-(6-(3-(S)-tetrahydrofuranyloxy)piperidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine

Prepared as described for Example 369; substituting (S)-3-hydroxytetrahydrofuran for benzyl alcohol.

15 MS (APCI+) m/z 465 (M+H)⁺;
¹H NMR (300 MHz, DMSO-d₆) δ 10.08 (bs, 1H), 8.93 (s, 1H), 8.52 (d, 1H), 8.51 (s, 1H), 7.98-7.40 (m, 6H), 5.80 (m, 1H), 4.05-3.78 (m, 4H), 2.36 (m, 1H), 2.15 (m, 1H)

20 Example 3814-amino-5-(3-bromophenyl)-7-(6-(trans-3-ethoxy-4-hydroxy)pyrrolidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine

The title compound was prepared as described for Example 367 substituting anti-3-ethoxy-4-hydroxypyrrrolidine (Chemical and Pharmaceutical Bulletin, 41, 1993, 132, Okada, T.) for (1S,4S)-2-aza-5-oxa-bicyclo[2.2.1]heptane, followed by treatment with 1M 25 HCl ether.

MS (APCI+) m/z 508 (M+H)⁺;
¹H NMR (300 MHz, DMSO-d₆) δ 10.12 (bs, 1H), 8.89 (s, 1H), 8.38 (d, 1H), 8.28 (s, 1H), 7.90-7.40 (m, 5H), 4.40-3.40 (m, 9H), 1.10 (t, 3H)

30 Example 382

4-amino-5-(3-bromophenyl)-7-(6-(cis-3-ethoxy-4-hydroxy)pyrrolidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine

Treatment of anti-N-Boc-3-ethoxy-4-hydroxypyrrrolidine (Chemical and Pharmaceutical Bulletin, 41, 1993, 132, Okada, T.) with triphenylphosphine, 4-nitrobenzoic acid and diethyl azodicarboxylate in THF at 0°C to room temperature gave a syn-N-Boc-3-ethoxy-4-(4'-nitrophenylcarbonyloxy)pyrrolidine. This was then hydrolyzed with sodium hydroxide in methanol to give syn-N-Boc-3-ethoxy-4-hydroxypyrrrolidine, which was subsequently deprotected with 4M HCl in dioxane to give syn-3-ethoxy-4-hydroxypyrrrolidine.

10 The title compound was prepared as described for Example 367 substituting syn-3-ethoxy-4-hydroxypyrrrolidine for (1S,4S)-2-aza-5-oxa-bicyclo[2.2.1]heptane, followed by treatment with 1M HCl ether.

MS (ESI+) m/z 508 (M+H)⁺;

¹H NMR (300 MHz, DMSO-d₆) δ 10.17 (bs, 1H), 8.91 (s, 1H), 8.38 (d, 1H), 8.28 (s, 1H), 7.91-7.79 (m, 2H), 7.67-7.49 (m, 4H), 4.80-3.50 (m, 9H), 1.39 (t, 3H)

Example 383

4-amino-5-(3-bromophenyl)-7-(6-(trans-3-ethoxy-4-hydroxy)pyrrolidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine

20 The title compound was prepared as described for Example 370 substituting anti-3-ethoxy-4-hydroxypyrrrolidine (Chemical and Pharmaceutical Bulletin, 41, 1993, 132, Okada, T.) for 4-methoxypiperidine, followed by treatment with 1M HCl ether.

MS (ESI+) m/z 507 (M+H)⁺;

¹H NMR (300 MHz, DMSO-d₆) δ 10.00 (bs, 1H), 9.03 (s, 1H), 8.87 (s, 1H), 8.74 (d, 1H), 8.23 (s, 1H), 7.97 (s, 1H), 7.80 (m, 1H), 7.59 (m, 2H), 7.36 (m, 1H), 7.11 (m, 1H), 4.40-3.00 (m, 9H), 1.10 (t, 3H)

Example 384

4-amino-5-(3-bromophenyl)-7-(6-(trans-3,4-bis-ethoxy)pyrrolidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine

30

Treatment of anti-N-Boc-3-ethoxy-4-hydroxypyrrolidine (Chemical and Pharmaceutical Bulletin, 41, 1993, 132, Okada, T.) with sodium hydride and ethyl iodide in anhydrous DMF gave anti-N-Boc-3,4-diethoxypyrrolidine, which was subsequently deprotected with 4M HCl in dioxane to give anti-3,4-diethoxypyrrolidine.

5 The title compound was prepared as described for Example 367 substituting anti-3,4-diethoxypyrrolidine for (1S,4S)-2-aza-5-oxa-bicyclo[2.2.1]heptane, followed by treatment with 1M HCl ether.

MS (FAB+) m/z 536 (M+H)⁺;

¹H NMR (300 MHz, DMSO-d₆) δ 10.18 (bs, 1H), 8.82 (s, 1H), 8.39 (d, 1H), 8.34 (s, 1H),

10 7.90 (m, 2H), 7.70-7.46 (m, 4H), 4.25 (m, 2H), 3.84 (m, 4H), 3.67 (m, 4H), 1.2 (t, 6H)

Example 385

4-amino-5-(3-bromophenyl)-7-(6-(trans-3,4-bis-ethoxy)pyrrolidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine

15 The title compound was prepared as described for Example 370 substituting anti-3,4-diethoxypyrrolidine (Example 382) for 4-methoxypiperidine, followed by treatment with 1M HCl ether.

MS (ESI+) m/z 535 (M+H)⁺;

¹H NMR (300 MHz, DMSO-d₆) δ 10.00 (bs, 1H), 9.03 (m, 1H), 8.87 (s, 1H), 8.71 (m, 1H),

20 8.22 (s, 1H), 7.95 (m, 1H), 7.80 (m, 1H), 7.58 (m, 2H), 7.35 (bs, 1H), 7.09 (m, 1H), 4.25-3.20 (m, 10H), 1.12 (t, 6H)

Example 386

4-amino-5-(3-bromophenyl)-7-(6-(cis-3,4-bis-ethoxy)pyrrolidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine

Treatment of N-benzyl-3-pyrroline with osmium tetroxide and N-methyl-morpholine-N-oxide in THF gave syn-N-Boc-3,4-dihydroxypyrrolidine, which was then treated with sodium hydride (5 eq.) and ethyl iodide (5 eq) in DMF to give syn-N-Boc-3,4-diethoxypyrrolidine. This was debenzylated under pressure in H₂ atmosphere to afford 30 syn-3,4-diethoxypyrrolidine.

The title compound was prepared as described for Example 370 substituting syn-3,4-dioxyppyrrolidine for 4-methoxypiperidine, followed by treatment with 1M HCl ether.

MS (ESI+) m/z 535 (M+H)⁺;

5 ¹H NMR (300 MHz, DMSO-d₆) δ 10.03 (bs, 1H), 9.03 (m, 1H), 8.89 (s, 1H), 8.74 (m, 1H), 8.25 (s, 1H), 7.95 (m, 1H), 7.62 (m, 1H), 7.60 (m, 2H), 7.39 (bs, 1H), 7.11 (m, 1H), 4.30-3.40 (m, 10H), 1.16 (t, 6H)

Example 387

10 4-amino-5-(3-bromophenyl)-7-(6-(cis-3,4-bis-ethoxy)pyrrolidinyl)-3-pyridazinyl)pyrido[2.3-d]pyrimidine

The title compound was prepared as described for Example 367 substituting syn-3,4-dioxyppyrrolidine (prepared in Example 384) for (1S,4S)-2-aza-5-oxa-bicyclo[2.2.1]heptane, followed by treatment with 1M HCl ether.

15 MS (ESI+) m/z 536.1 (M+H)⁺;
¹H NMR (300 MHz, DMSO-d₆) δ 10.13 (bs, 1H), 8.87 (s, 1H), 8.35 (d, 1H), 8.28 (s, 1H), 7.82 (m, 2H), 7.63-7.40 (m, 4H), 4.40-3.40 (m, 10H), 1.16 (t, 6H)

Example 388

20 4-amino-5-(3-bromophenyl)-7-(6-(cis-3-ethoxy-4-hydroxy)pyrrolidinyl)-3-pyridyl)pyrido[2.3-d]pyrimidine

The title compound was prepared as described for Example 370 substituting syn-3-ethoxy-4-hydroxyppyrrolidine (prepared as in Example 382) for 4-methoxypiperidine, followed by treatment with 1M HCl ether.

25 MS (ESI+) m/z 507 (M+H)⁺;
¹H NMR (300 MHz, DMSO-d₆) δ 10.00 (bs, 1H), 9.02 (m, 1H), 8.88 (s, 1H), 8.72 (m, 1H), 8.22 (s, 1H), 7.97 (m, 1H), 7.81 (m, 1H), 7.60 (m, 2H), 7.39 (bs, 1H), 7.17 (m, 1H), 4.40-3.40 (m, 9H), 1.17 (t, 3H)

4-amino-5-(3-bromophenyl)-7-(6-(cis-3-amino-4-hydroxy)pyrrolidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine

Syn-N-benzyl-3-hydroxy-4-(t-butylcarbonylamy)pyrrolidine was made by Sharpless method (JACS 120 1998 1215, Sharpless, K.B.; Tetrahedron asymmetry 5(7) 1994 1333, Saigo K.). This was debenzylated under H₂ to give syn-3-hydroxy-4-(t-butylcarbonylamy)pyrrolidine.

The title compound was prepared as described for Example 367 substituting syn-3-hydroxy-4-(t-butylcarbonylamy)pyrrolidine for (1S,4S)-2-aza-5-oxa-bicyclo[2.2.1]heptane, followed by treatment with 4M HCl dioxane.

10 MS (ESI+) m/z 479.2 (M+H)⁺;
¹H NMR (300 MHz, DMSO-d₆) δ 10.07 (bs, 1H), 8.94 (s, 1H), 8.59 (bs, 2H), 8.35 (m, 2H), 7.85 (m, 2H), 7.70-7.30 (m, 4H), 4.70-3.20 (m, 9H)

Example 390 4-amino-5-(3-bromophenyl)-7-(6-(cis-3-amino-4-hydroxy)pyrrolidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine

15 The title compound was prepared as described for Example 370 substituting syn-3-hydroxy-4-(t-butylcarbonylamy)pyrrolidine (prepared in Example 389) for 4-methoxypiperidine, followed by treatment with 4M HCl dioxane.
MS (APCI+) m/z 478 (M+H)⁺;
20 ¹H NMR (300 MHz, DMSO-d₆) δ 10.07 (bs, 1H), 9.08 (m, 1H), 8.88 (s, 1H), 8.64 (m, 3H), 8.21 (s, 1H), 7.97 (s, 1H), 7.82 (m, 1H), 7.60 (m, 2H), 7.36 (m, 1H), 7.03 (m, 1H), 4.65-3.65 (m, 9H)

Example 391

25 4-amino-5-(2-pyridyl)-7-(6-(1,4-dioxa-8-azaspiro[4.5]decan-8-yl)-3-pyridyl)pyrido[2,3-d]pyrimidine

Prepared according to the procedure of Example 392, except substituting 5-acetyl-2-(1,4-dioxa-8-azaspiro[4.5]decan-8-yl)pyridine for 5-acetyl-2-morpholinyipyridine, and 3-pyridinecarboxaldehyde for 2,3-dichlorobenzaldehyde. The treatment with HCl/ethanol to form the hydrochloride salt was omitted, and the free base was obtained instead. IR

(MIC) 3500, 3310, 3100, 2982, 1605, 1580, 1555, 1512, 1351, 1238, 1100cm⁻¹; MS m/z 442 (M+H)⁺

Example 392

5 4-amino-5-(2,3-dichlorophenyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine
4-(2,3-Dichlorophenyl)-3-cyano-6-(6-morpholinyl-3-pyridyl)pyridine-2-amine
(0.47 g) and ammonium sulfate (20 mg) was dissolved in triethylorthoformate (25 ml) and
heated to reflux for about 6.5 hours. The reaction mixture was cooled to room temperature,
and a 2 M solution of ammonia in ethanol (50 ml) was added. The reaction was stirred at
10 room temperature for about 18 hours, then heated to reflux for about 6 hours, and then
cooled again to room temperature. The solvents were removed under vacuum. The residue
was purified by flash chromatography eluting with 5% of 19:1 ethanol:ammonium
hydroxide in ethyl acetate, and then converted to the hydrochloride salt by treatment with
HCl/EtOH, followed by removal of solvent and titration with ether to give the title
15 compound.
IR (MIC) 3355, 2980, 1644, 1602, 1437, 1369, 1250cm⁻¹;
MS m/z 453 (M+H)⁺

Step a 4-(2,3-dichlorophenyl)-3-cyano-6-(6-morpholinyl-3-pyridyl)pyridine-2-amine

20 Malononitrile (0.33 g) and 2,3-dichlorobenzaldehyde (0.88 g) were dissolved in
1,2-dichloroethane, and 1-2 drops of triethylamine were added. The reaction was stirred at
room temperature for about 2.5 hours, then 5-acetyl-2-morpholinylpyridine (0.62 g) and
ammonium acetate (2.31 g) were added. The reaction was heated to reflux for about 5
hours, then cooled to room temperature. The reaction mixture was purified by flash
25 chromatography eluting with 30% EtOAc/Hexanes.

Example 393

4-amino-5-(2-pyridyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine

Prepared according to the procedure of Example 392 except substituting 3-
30 pyridinecarboxaldehyde for 2,3-dichlorobenzaldehyde.

IR (MIC) 3050, 1650, 1603, 1540, 1440, 1375, 1252cm⁻¹;

MS m/z 386 (M+H)⁺

Example 394

5 4-amino-5-(2-ethoxyphenyl)-7-(6-(1,4-dioxa-8-azaspiro[4.5]decan-8-yl)-3-pyridyl)pyrido[2,3-d]pyrimidine

Prepared according to the procedure of Example 392, except substituting 5-acetyl-2-(1,4-dioxa-8-azaspiro[4.5]decan-8-yl)pyridine for 5-acetyl-2-morpholinylpyridine, and 2-ethoxybenzaldehyde for 2,3-dichlorobenzaldehyde. The treatment with HCl/ethanol to form the hydrochloride salt was omitted, and the free base was obtained instead.

10 IR (MIC) 3480, 3060, 1738, 1640, 1600, 1560, 1537, 1500, 1345, 1230, 1220, 1100cm⁻¹;

MS m/z 485 (M+H)⁺

Example 395

15 4-amino-5-(2-bromo-5-ethoxyphenyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine

Prepared according to the procedure of Example 392, except substituting 2-methoxy-5-bromobenzaldehyde for 2,3-dichlorobenzaldehyde.

IR (MIC) 3440, 2975, 1642, 1600, 1490, 1440, 1370, 1250cm⁻¹;

20 MS m/z 493 (M+H)⁺

Example 396

4-amino-5-(2,5-dichlorophenyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine

4-(2,5-dichlorophenyl)-3-cyano-6-(6-morpholinyl-3-pyridyl)pyridine-2-amine

25 (0.28 g) and ammonium sulfate (10 mg) were dissolved in triethylorthoformate (10 ml) and heated to reflux for about 4 hours. The reaction mixture was cooled to room temperature, and a 2 M solution of ammonia in ethanol (20 ml) was added. The reaction was stirred at room temperature for about 18 hours, then a solution of 1 M sodium methoxide in methanol (5 ml) was added. The reaction was heated to reflux for about 2.5 hours, and then cooled again to room temperature. The reaction mixture was neutralized

with a solution of 1 N aqueous HCl (5 ml) and the solvents were removed under vacuum. The residue was purified by flash chromatography eluting with 2.5% of 19:1 ethanol:ammonium hydroxide in ethyl acetate, and then converted to the hydrochloride salt by treatment with HCl/EtOH, followed by removal of solvent and titration with ether 5 to give the title compound.

IR (MIC) 3480, 3060, 1640, 1600, 1580, 1440, 1371, 1260, 1239cm⁻¹;
MS m/z 453.2 (M+H)⁺

The 4-(2,5-dichlorophenyl)-3-cyano-6-(6-morpholinyl-3-pyridyl)pyridine-2-amine was prepared following the conditions given under Example 392 except substituting 2,5-10 dichlorobenzaldehyde for 2,3-dichlorobenzaldehyde.

Example 397

4-amino-5-(2,5-dimethylphenyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine

Prepared according to the procedure of Example 396, except substituting 2,5-15 dimethylbenzaldehyde for 2,5-dichlorobenzaldehyde.

IR (MIC) 3420, 2910, 1640, 1600, 1580, 1240cm⁻¹;
MS m/z 413.2 (M+H)⁺

Example 399

20 4-amino-5-(3-fluorophenyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine
Prepared according to the procedure of Example 396, except substituting 3-fluorobenzaldehyde for 2,5-dichlorobenzaldehyde.

IR (KBr) 3480, 1672, 1639, 1617, 1480, 1421, 1315, 1305cm⁻¹;
MS m/z 403 (M+H)⁺

25

Example 400

4-amino-5-(3-trifluoromethylphenyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine
Prepared according to the procedure of Example 396, except substituting 3-trifluoromethylbenzaldehyde for 2,5-dichlorobenzaldehyde.

30 IR (MIC) 3000, 1641, 1600, 1440, 1369, 1324, 1239, 1120cm⁻¹;

MS m/z 453 (M+H)⁺Example 4014-amino-5-(3-fluoro-5-trifluoromethylphenyl)-7-(6-(1,4-dioxa-8-azaspiro[4.5]decan-8-yl)-5 3-pyridyl)pyrido[2,3-d]pyrimidine

Prepared according to the procedure of Example 327, substituting 3-fluoro-5-trifluoromethylbenzaldehyde for 3-bromobenzaldehyde.

mp: unmelted at 300°C;

MS (FAB)⁺ m/z calc'd for C₂₆H₂₃N₆O₂F₄: 527.1813, found 527.1810.

10 IR (cm⁻¹): 3314, 3081, 1580, 1558, 1515, 1428, 1357, 1329, 1238, 1139, 1106.Example 4024-amino-5-(3,5-dichlorophenyl)-7-(6-(1,4-dioxa-8-azaspiro[4.5]decan-8-yl)-3-pyridyl)pyrido[2,3-d]pyrimidine

15 Prepared according to the procedure of Example 327, except substituting 3,5-dichlorobenzaldehyde for 3-bromobenzaldehyde.

mp: unmelted at 300°C;

MS (FAB)⁺ m/z calc'd for C₂₅H₂₃N₆O₂Cl₂: 509.1254, found: 509.1246

IR (cm⁻¹): 3487, 3299, 3065, 1578, 1556, 1515, 1431, 1354, 1238, 1104.

20

Example 4034-amino-5-(3-bromophenyl)-7-(6-(1,5-dioxa-9-azaspiro[5.5]undecan-9-yl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine

25 Prepared according to the procedure of Example 367, except substituting 1,5-dioxa-9-azaspiro[5.5]undecane for (1S,4S)-2-aza-5-oxa-bicyclo[2.2.1]heptane.

mp: 8 190°C;

MS (FAB)⁺ m/z calc'd for C₂₅H₂₃N₆O₂⁸¹Br: 536.1233, found: 536.1233.

IR (cm⁻¹): 3471, 3297, 3059, 2961, 1579, 1562, 1461, 1407, 1354, 1236, 1104.

30

Example 404

4-amino-5-(4-bromo-2-thienyl)-7-(6-(1,4-dioxa-8-azaspiro[4.5]decan-8-yl)-3-pyridyl)pyrido[2,3-d]pyrimidine

Prepared according to the procedure of Example 327, substituting 4-bromothiophene-2-carboxaldehyde for 3-bromobenzaldehyde.

5 mp: δ 245°C;

MS (FAB)⁺ m/z calc'd for C₂₃H₂₂N₆O₂S⁷⁹Br: 525.0703, found: 525.0699.

IR (cm⁻¹): 3477, 3296, 3094, 1603, 1579, 1556, 1511, 1428, 1352, 1239, 1104.

Example 405

10 4-amino-5-(3-bromophenyl)-7-(6-(4-tertbutyl)piperidinyl-3-pyridazinyl)pyrido[2,3-d]pyrimidine

Prepared by the method of Example 367, substituting 4-tertbutylpiperidine for (1S,4S)-2-aza-5-oxa-bicyclo[2.2.1]heptane.

mp: δ > 270°C;

15 MS (FAB)⁺ m/z calc'd for C₂₆H₂₉N⁷⁹Br: 520.1647, found: 520.1652.

IR (cm⁻¹): 3474, 3298, 3085, 2952, 1578, 1553, 1461, 1405, 1351, 1254, 1191, 1159.

Example 406

20 4-amino-5-(3-bromophenyl)-7-(6-(4-N-formyl)piperidinyl-3-pyridazinyl)pyrido[2,3-d]pyrimidine

2-Amino-4-(3-bromophenyl)-3-cyano-6-(6-chloro-3-pyridazinyl)pyridine (310mg), prepared in Example 367, and 1,3-propylenedioxypiperidine (354mg) were dissolved into DMSO (2.5ml) and stirred 48 hours. The reaction mixture was partitioned between 0.4M pH7 aqueous potassium phosphate buffer and worked up as usual. The intermediate was suspended in

25 formamide (15ml) and o-dichlorobenzene (7ml) and heated at 200°C for 2.5h. The reaction mixture was partitioned between salt water and dichlomethane, and the organic phase was separated, filtered through celite, and worked up as usual. Chromatographed (MeOH/EtOAc/CH₂Cl₂).

mp: δ 190°C;

30 MS (FAB)⁺ m/z calc'd for C₂₃H₂₂N₆O₂⁹Br: 505.1094, found: 505.1095.

IR (cm⁻¹): 3472, 3299, 1654, 1578, 1555, 1478, 1418, 1354, 1225.

Example 407

4-amino-5-(3-bromo-2-thienyl)-7-(6-(4,4-ethylenedioxypiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine

5

Prepared by the method of Example 327, substituting 3-bromothiophene-2-carboxaldehyde for 3-bromobenzaldehyde.

mp: δ 230°C;

MS (FAB)⁺ m/z calc'd for C₂₃H₂₂N₆O₂S⁷⁹Br: 527.0688, found: 527.0692.

10 IR (cm⁻¹): 3472, 3297, 3091, 1611, 1581, 1557, 1519, 1428, 1351, 1334, 1229, 1112.

Example 408

4-amino-5-(3-cyanophenyl)-7-(6-morpholinyl-3-pyridazinyl)pyrido[2,3-d]pyrimidine

A formamide complex of Example 134 (762mg), Zn(CN)₂ (94mg), and Pd(PPh₃)₄ (173mg) 15 were heated in DMF (5ml) at 105°C for 3h 40m. The reaction mixture was partitioned between CH₂Cl₂ and water and worked up as usual. Recrystallization of the crude solid from CHCl₃ gave the title compound.

mp: δ 3 290°C;

MS (FAB)⁺ m/z calc'd for C₂₃H₂₀N₆O: 410.1724, found: 410.1722.

20 IR (cm⁻¹): 3482, 3313, 2232, 1588, 1542, 1507, 1357, 1240.

Example 409

4-amino-5-(3-Bromophenyl)-7-(6-(S-O-ethyl-2-hydroxymethylpyrrolidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine

25

Prepared by the method of Example 367, substituting (S)-O-ethyl-2-hydroxymethylpyrrolidine for (1S,4S)-2-aza-5-oxa-bicyclo[2.2.1]heptane.

mp: δ 3 180°C;

MS (FAB)⁺ m/z calc'd for C₂₄H₂₅N₇O₈⁷⁹Br: 508.1283, found: 508.1285.

30 IR (cm⁻¹) of salt: 3438, 3302, 2974, 1637, 1609, 1588, 1554, 1440, 1374, 1111.

Step a. (S)-O-ethyl-2-hydroxymethylpyrrolidine

A suspension of (S)-N-tertbutyloxycarbonyl-2-hydroxymethylpyrrolidine (1006mg) and crushed NaOH (800mg) in DMSO (20ml) was treated with ethyl iodide (560ml). After the 5 suspension had been stirred for 45m, the reaction mixture was partitioned between 0.2M aq KH₂PO₄ and Et₂O, worked up as usual, and concentrated. A solution of the intermediate (1.04g) in MeOH (10ml) was treated with conc aq HCl (1.5ml) and stirred over the weekend. The reaction mixture was concentrated and partitioned between 3M aq K₂PO₄ and Et₂O, worked up as usual, and concentrated to give the desired amine

10

Example 410

4-amino-5-(3-bromophenyl)-7-((2S,3S)-2,3-dimethyl-1,4-dioxa-8-azaspiro[4.5]decan-8-yl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine

Prepared by the method of Example 327, substituting (2S,3S)-2,3-dimethyl-1,4-dioxa-8-15 azaspiro[4.5]decan for 4,4-ethylenedioxypiperidine and using 1,2,4-trichlorobenzene as cosolvent with formamide at 200°C in the final cyclization.
mp: δ >235°C; MS (FAB)⁺ m/z calc'd for C₂₆H₂₇N₂O₂⁸¹Br: 550.1389, found: 550.1374.
IR (cm⁻¹): 3477, 3046, 2968, 1578, 1559, 1460, 1410, 1353, 1251, 1113.

20 410a. 4,4-(1S,2S-dimethylethanedioxy)piperidine

N-tertbutyloxycarbonylpiperidi-N-4-one (2.59g), (2S,3S)-butanediol (1.464g), and a catalytic amount of p-toluenesulphonic acid were dissolved into benzene (25ml) within a flask fitted with a Dean-Stark trap and condenser, and refluxed 1 day. The reaction mixture was partitioned between aq NaHCO₃ and ether, and worked up as usual. Chromatographed (CH₃CN/CH₂Cl₂). This 25 intermediate (3.78g) was dissolved into CH₂Cl₂ (10ml) and treated with TFA (3ml). After 90m more TFA (0.5ml) was added, and after another 90min the reaction mixture was concentrated, then conc'd from CHCl₃, then from toluene. The intermediate, 6-acetyl-3-chloropyridazine (2.03g), and diisopropylethylamine (9.75ml) were dissolved into methanol (55ml) and heated at 55°C for 2d. The reaction mixture was added to Et₂O and 1M pH7 aq potassium phosphate buffer 30 and worked up as usual. Purified by column chromatography (EtOAc/Hexanes).

Example 4114-amino-5-(3-bromophenyl)-7-(6-(4,4-(cis-1,2-dioxycyclopentyl)piperidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine

5 Prepared by the method of Example 410 (A-312378), substituting cis-1,2-dihydroxycyclopentane for (2S,3S)-butanediol.

mp: unmelted at 300°C;

MS (FAB)⁺ m/z calc'd for C₂₇H₂₇N₃O₂⁸¹Br: 562.1389, found: 562.1382.

IR (cm⁻¹): 3478, 3081, 2959, 1578, 1560, 1460, 1406, 1351, 1246, 1109.

10

Example 4124-amino-5-(3-bromophenyl)-7-(6-(4-acetyl-1-oxa-4,8-diazaspiro[4.5]decan-8-yl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine

4-Acetyl-1-oxa-4,8-diazaspiro[4.5]decano (341mg) was dissolved into CH₂Cl₂ (0.5ml) and 15 treated with TFA (1ml). After 20m the reaction mixture was concentrated. The intermediate, potassium carbonate (552mg), and 4-amino-5-(3-bromophenyl)-7-(6-chloropyridaz-3-yl)pyrido[2,3-d]pyrimidine (165mg), prepared in Example 367, were suspended in DMSO (2ml) and heated 6h at 120°C. The reaction mixture was partitioned between brine and CH₂Cl₂ and worked up as usual. Purification by chromatography (CH₃OH/CH₃CN/CH₂Cl₂) provided the title 20 compound..

mp: dec 260°C (sweats and turns deep brown 220°C); MS (FAB)⁺ m/z calc'd for C₂₆H₂₆N₃O₂⁸¹Br: 563.1342, found: 563.1329.

IR (cm⁻¹): 3487, 3308, 1626, 1578, 1553, 1461, 1416, 1353, 1254, 1073.

25 412a.

N-tertbutyloxycarbonyl-4-oxopiperidine (996mg) and 2-aminoethanol (320ml) were dissolved into ethanol (5ml). After 4h, the reaction mixture was concentrated. and the residue dissolved into CH₂Cl₂ (8ml) and pyridine (2ml). Acetyl chloride (360ml) was added and the mixture was stirred overnight. More acetyl chloride (350ml) was added then and the same 30 amount 2h later. After 15m more, the reaction mixture was quenched with aq NaHCO₃ and

worked up as usual but with NaHCO₃ and NaCl in each aqueous wash. This intermediate was purified by chromatography (EtOAc/Hexanes).

Example 413

5 4-amino-5-(3-bromophenyl)-7-(6-(2R,3R)-2,3-bis(methoxymethyl)-1,4-dioxa-8-azaspiro[4.5]decan-8-yl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine

Prepared following the procedure according to Example 412 (A-314908), substituting (2R,3R)-2,3-bis(methoxymethyl)-1,4-dioxa-8-azaspiro[4.5]decan-8-yl for 412a.

mp: 8 >130°C; MS (FAB)⁺ m/z calc'd for C₂₈H₃₁N₃O₄⁷⁹Br: 608.1615, found: 608.1614.

10 IR (cm⁻¹): 3486, 3304, 2928, 1578, 1554, 1461, 1407, 1352, 1235, 1106.

Example 414

4-amino-5-(3-bromophenyl)-7-(6-(4,4-(cis-3,4-dioxy-oxacyclopentyl)piperidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine

15 Prepared following the procedure of Example 412 (A-314908), substituting 4,4-(cis-3,4-dioxy-oxacyclopentane)piperidine for 412a.

mp: 8 > 280°C; MS (FAB)⁺ m/z calc'd for C₂₆H₂₃N₃O₃⁷⁹Br: 562.1202, found: 562.1209.

IR (cm⁻¹): 3475, 3293, 3094, 1577, 1559, 1461, 1410, 1355, 1229, 1111.

Example 415

4-amino-5-(3-bromophenyl)-7-(6-(3-methoxy-1,5-dioxa-9-azaspiro[5.5]undecan-9-yl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine

Prepared following the procedure of Example 412 (A-314908), substituting 3-methoxy-1,5-dioxa-9-azaspiro[5.5]undecane for 412a.

25 mp: 8 > 275°C; MS (FAB)⁺ m/z calc'd for C₂₈H₂₇N₃O₃⁷⁹Br: 564.1359, found: 564.1354.
IR (cm⁻¹): 3478, 3293, 3070, 1574, 1564, 1462, 1407, 1349, 1227, 1147, 1101.

Example 416

4-amino-5-(3-bromophenyl)-7-(6-(1,5-dioxa-3-hydroxymethyl-9-azaspiro[5.5]undecan-9-yl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine

30

Prepared following the procedure of Example 412, substituting 1,5-dioxa-3-hydroxymethyl-9-azaspiro[5.5]undecane for 412a, and adding butanol during the work-up.
mp: unmelted at 300°C (sweats/shrivels >270°C); MS (ESI)⁺ m/z: 564/566.
IR (cm⁻¹): 3475, 3302, 1578, 1554, 1462, 1409, 1354, 1237, 1146, 1100.

5

Example 4174-amino-5-(3-bromophenyl)-7-(6-(1,7,14-trioxa-11-azadispiro[4.2.5.2]pentadecan-11-yl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine

Prepared following the procedure of Example 412 (A-314908), substituting 1,7,14-trioxa-11-azadispiro[4.2.5.2]pentadecane for 412a.
10 mp: unmelted at 300°C; MS (ESI)⁺ m/z: 590/592.
IR (cm⁻¹): 3476, 3295, 3087, 2968, 1577, 1562, 1465, 1419, 1356, 1149, 1099.

Example 41815 4-amino-5-(4-tetrahydropyranyl)-7-(4,4-ethylenedioxypiperidinyl)pyrido[2,3-d]pyrimidine

Prepared following the procedure according to Example 327, substituting 1,1-dicyano-3-(4-tetrahydropyranyl)ethene from Example 292 for 3-bromobenzaldehyde, and 6-acetyl-3-chloropyridazine for 5-acetyl-2-chloropyridine at room temperature rather than reflux.
mp: unmelted at 300°C; MS (FAB)⁺ m/z calc'd for C₂₂H₂₇N₃O₃: 450.2254, found: 450.2266.
20 IR (cm⁻¹): 3544, 3304, 2938, 1579, 1557, 1468, 1415, 1355, 1240, 1104.

Example 4194-amino-5-(3-bromophenyl)-7-(6-(4-morpholinyliminopiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine

25 Prepared as described for Example 359; substituting 4-aminomorpholine for ethoxylamine hydrochloride.
MS (DCI/NH₃) m/z 559 (M+H)⁺;
IR (cm⁻¹): 1643, 1602, 1557.

30

Example 420

4-amino-5-(3-bromophenyl)-7-(6-(4-(N-methylpiperazinyl)iminopiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine

Prepared as described for Example 419 except substituting 1-amino- 4-N-methylpiperazine for 1-aminomorpholine.

5 MS (DCI) m/e 572 (M+H⁺;

IR 1647, 1602, 1559.

Example 421

4-amino-5-(3-bromophenyl)-7-(6-(4-(1,2,4-triazol-1-yl)iminopiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine

10 MS (DCI) m/e 541 (M+H⁺;

Prepared as described for Example 419 except substituting 4-amino- 1,2,4-triazole for 1-aminomorpholine

MS (DCI) m/e 541 (M+H⁺;

IR 1602, 1580.

15

Example 422

4-amino-5-(3-indolyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine

The title compound was prepared following the procedure of Example 396 except substituting 3-indolylcarboxaldehyde for 2,5-dichlorobenzaldehyde.

20 MS (DCI), m/z 424.

^H NMR (DMSO-d₆) d, 11.81 (s, 1H), 9.05 (d, 1H), 8.5 (s, 1H), 8.45 (dd, 1H), 7.84 (s, 2H), 7.55 (d, 1H), 7.40 (d, 1H), 7.25 (t, 1H), 7.10 (t, 1H), 6.58 (d, 1H), 3.72 (m, 4H), 3.6 (m, 4H).

25

Example 423

4-amino-5-(5-indolyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine

The title compound was prepared following the procedure of Example 422 except substituting 5-indolylcarboxaldehyde for 3-indolylcarboxaldehyde, which was prepared according to the procedure of Moyer et. al. Journal of Organic Chemistry, 51, 5106-5110,

30 1986.

MS (DCI). m/z 452.

IR (mic. cm⁻¹) 3448, 1557, 1503, 1234, 943.

Example 424

5 4-amino-5-(3-bromophenyl)-7-(6-(4-ethylpiperidinylcarboxylate)-3-pyridyl)pyrido[2,3-d]pyrimidine

Prepared following the procedures of Example 327 except substituting ethyl 4-piperidinecarboxylate for 4,4-ethlenedioxypiperidine.

MS (DCI) m/e 533 (M+H)⁺;

10 IR (mic.,cm⁻¹) 1604, 1592, 1560

Example 425

4-amino-5-(3-bromophenyl)-7-(2-phenylmethyl-3(2H)-pyridazinone-6-yl)pyrido[2,3-d]pyrimidine

15 step a 3-acetyl-6-hydroxypyridazine

A solution of 3-acetyl-6-chloropyridazine (prepared in Example 246 step b)(6.0 g, 38.4 mmol) and aq. 3N HCl (70 mmol) in THF (100 mL) was heated at 60°C for 4 h, cooled to ambient temperature, concentrated and chromatographed on silica gel (30% EtOAc-hexane) to obtain the desired compound (3.3 g, 62%). ¹H NMR (CDCl₃, 300 MHz) δ 12.42 (broad s, 1H), 7.98 (d, J=9.0 Hz, 1H), 7.02 (d, J=9.0 Hz, 1H), 2.58 (s, 3H); MS m/z (DCI) 139 (M+H)⁺.

step b 6-acetyl-2-phenylmethyl-3(2H)-pyridazinone

25 A solution of 3-acetyl-6-hydroxypyridazine (2.9 g, 21.0 mmol), benzyl bromide (2.8 mL, 23.0 mmol) and KOH (1.3 g, 23.0 mmol) in DMF (45 mL) was stirred at ambient temperature for 15 h. The mixture was diluted with EtOAc and washed twice with water. Aqueous layer was extracted with EtOAc and combined organic fractions concentrated and chromatographed (10-25%EtOAc-hexane) to obtain of the desired 6-acetyl-2-phenylmethyl-3(2H)-pyridazinone (3.6 g, 75%) as an oil. ¹H NMR (CDCl₃, 300

MHz) δ 7.80 (d, J=9.2 Hz, 1H), 7.48-7.27 (m, 5H), 6.90 (d, J=9.2 Hz, 1H), 5.38 (s, 2H). 2.51 (s, 3H); MS m/z (DCI) 229 (M+H)⁺.

The title compound was prepared as described in Example 327 except substituting 6-acetyl-2-phenylmethyl-3(2H)-pyridazinone for 3-acetyl-(4,4-5 ethylenedioxypiperidinyl)pyridine

MS (DCI) m/e 485 (M+H⁺);
IR 1640, 1618, 1560.

Example 426

10 4-amino-5-(3-bromophenyl)-7-(6-(4-(morpholinylcarboxamide)piperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine

The title compound was prepared following the procedure of Example 424 except substituting 3-acetyl-6-(4-N-morpholinylcarboxamide)piperidinyl)pyridine for ethyl-4-piperidinecarboxylate derivative.

15 MS (ESI+), m/z 575 (M+H)⁺;
IR (MIC); cm⁻¹, 3486, 1557, 1211, 933.

3-acetyl-6-(4-N-morpholinylcarboxamide)piperidinyl)pyridine:

20 2-chloro-5-acetylpyridine (6g) and ethyl isonipeptate (6.1g) was refluxed in ethanol. The volatiles were evaporated to leave 2-(1'-ethyl isonipeptate)-4-acetylpyridine. This material was treated with aqueous lithium hydroxide, followed by acidification and filtration. The resulting acid (1.5 g) was treated with morpholine (2.4 g), hydroxybenzotriazole (1.3g) and 1-(3-Dimethylaminopropyl)-3-carbodiimide, to afford the desired compound .

25 MS (DCI) m/z, 318 (M+H)⁺.

Example 427

4-amino-5-(3-bromophenyl)-7-(6-(4-(N-morpholinylaminocarboxamide)piperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine

Prepared following the procedure of Example 426 except substituting 4-aminomorpholine for morpholine.

MS (ESI) m/z 589 (M+H)⁺;

IR (cm⁻¹) 3490, 1557, 1351, 1111.

5

Example 428

4-amino-5-(3-bromophenyl)-7-(6-(4-(N,N-dimethylaminocarboxamide)piperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine

10 Prepared following the procedure of Example 426 except substituting dimethylamine for morpholine.

MS (ESI) mz 532 (M+H)⁺;

H¹ NMR (300 MHz; DMSO-d₆, δ 9.05 (d, 1H), 8.52 (s, 1H), 8.44 (dd, 1H), 7.85 (s, 2H), 7.78 (dt, 1H), 7.55 (s, 1H), 6.99 (d, 1H), 4.49 (d, 2H), 3.09 (s, 2H), 3.00 (m, 3H), 2.80 (s, 15 3H), 1.7 (m, 2H), 1.54 (m, 2H).

Example 429

4-amino-5-(3-bromophenyl)-7-(6-(4-(N-methyl-N-methoxyethylcarboxamide)piperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine

20 Prepared following the procedure of Example 426 except substituting N-methyl-N-methoxyethylamine for morpholine..

MS (ESI+) m/z 576, (M+H)⁺;

IR (mic, cm⁻¹) 3489, 1555, 1118, 936.

25

Example 430

4-amino-5-(4-quinolyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine

Prepared following the procedure of 392, substituting 4-quinolincarboxaldehyde for 2,3-dichlorobenzaldehyde.

MS (ESI+), m/z 436 (M+H)⁺;

30 IR (mic., cm⁻¹) 3488, 1580, 1557, 1227, 936.

Example 4314-amino-5-(3-bromophenyl)-7-(6-(4-(N-methoxyethyl)carboxamide)piperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine

5 Prepared following the procedure of Example 426, except substituting N-methoxyethylamine for morpholine...

MS (ESI+) M/z 564, (M+H)⁺;

IR (cm⁻¹) 3310, 1560, 1210, 954.

Example 4324-amino-5-(3-bromophenyl)-7-(6-(4-hydroxymethyl)piperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine

Prepared as described for Example 370 except substituting 4-hydroxypiperidinepiperidine for 4-methoxypiperidine, which was prepared as follows:

15 ethyl isonipecotate (10g) was treated with lithium aluminum hydride (2.53g) in tetrahydrofuran for 36 hours.

MS. (ESI+) m/z 491 (M+H)⁺.

Example 4334-amino-5-(2-bromophenyl)-7-(6-(1,4-dioxa-8-azaspiro[4.5]decan-8-yl)-3-pyridyl)pyrido[2,3-d]pyrimidine

Prepared as described for Example 370 except substituting 1,4-dioxa-8-azaspiro[4.5]decan for 4-methoxypiperidine and substituting the dicyanostyrene derived from 2-bromobenzaldehyde instead of the 3-bromoderivative.

25 ¹H NMR (300 MHz, d₆-DMSO) δ 9.05 (d, 1H), 8.53 (s, 1H), 8.44 (dd, 1H), 7.91 (d, 1H), 7.83 (s, 1H), 7.66 (d, 2H), 7.56 (m, 1H), 7.04 (d, 1H), 3.93 (s, 3H), 3.77 (m, 4H), 1.67 (m, 4H);

MS (ESI) m/z 519/521 (M⁺+H, ⁷⁹Br/⁸¹Br).

Example 434

4-amino-5-(2-bromophenyl)-7-(6-(4-hydroxypiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine

Prepared as described for Example 433 except substituting 4-hydroxypiperidine for 4,4-ethylenedioxypiperidinc. IR (KBr pellet) ν_{max} 3485, 3298, 3198, 2938, 2848, 1600, 5 1574, 1557, 1357, 1225, 1024, 766 cm^{-1} ; MS (ESI) m/z 477/479 (M^++H , $^{79}\text{Br}/^{81}\text{Br}$).

Example 435

4-amino-5-(3-bromophenyl)-7-(6-(4-N-acetylpirerazinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine

Prepared as described for Example 370 except substituting 1-acetylpirerazine for 4-methoxypiperidine.

^1H NMR (300 MHz, d_6 -DMSO) δ 9.09 (d, 1H), 8.53 (s, 1H), 8.48 (dd, 1H), 7.86 (s, 1H), 7.85 (s, 1H), 7.78 (dt, 1H), 7.54 (m, 2H), 7.00 (d, 1H), 3.63-3.73 (m, 4H), 3.55-3.59 (m, 15 4H), 2.06 (s, 3H); MS (ESI) m/z 504/506 (M^++H , $^{79}\text{Br}/^{81}\text{Br}$).

Example 436

4-amino-5-(3-bromophenyl)-7-(6-(4-cyanopiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine

Prepared as described for Example 370 except substituting 4-cyanopiperidine for 4-methoxypiperidine, which was prepared as follows: isonicotamide was heated in POCl_3 at reflux for 2 hours and then was cooled to rt. Most of the POCl_3 was removed in vacuo, and the remaining syrup was carefully quenched with ice. The melted aqueous solution was extracted with CH_2Cl_2 , and the combined organic extracts were dried over Na_2SO_4 . Removal of the solvent in vacuo afforded 4-cyanopiperidine as a grey-white semi-solid.

^1H NMR (300 MHz, d_6 -DMSO) δ 9.07 (d, 1H), 8.53 (s, 1H), 8.45 (dd, 1H), 7.85 (m, 2H), 7.76-7.80 (m, 1H), 7.52 (m, 2H), 7.02 (d, 1H), 3.95-4.02 (m, 2H), 3.46-3.55 (m, 2H), 3.17 (m, 1H), 1.94-1.99 (m, 2H), 1.74-1.80 (m, 2H); 30 MS (ESI) m/z 486/488 (M^++H , $^{79}\text{Br}/^{81}\text{Br}$).

Example 4374-amino-5-(3-bromophenyl)-7-(6-(4-N-(4-fluorophenyl)piperazinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine

5 Prepared as described for Example 370 except substituting 1-(4-fluorophenyl)piperazine for 4-methoxypiperidine.

¹H NMR (300 MHz, d₆-DMSO) δ 9.10 (d, 1H), 8.53 (s, 1H), 8.48 (dd, 1H), 7.85 (m, 2H), 7.78 (dt, 1H), 7.55 (m, 2H), 7.00-7.11 (m, 5H), 3.81 (m, 4H), 3.21 (m, 4H);

MS (ESI) m/z 556/558 (M⁺+H, ⁷⁵Br/⁸¹Br).

10

Example 4384-amino-5-(4-fluorophenyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine

Prepared as described for Example 370 except substituting morpholine for 4-methoxypiperidine and substituting the dicyanostyrene derived from 4-fluorobenzaldehyde instead of the 3-bromoderivative.

¹H NMR (300 MHz, d₆-DMSO) δ 9.08 (d, 1H), 8.53 (s, 1H), 8.47 (dd, 1H), 7.83 (s, 1H), 7.65 (m, 2H), 7.44 (m, 2H), 6.99 (d, 1H), 3.59-3.73 (m, 8H);
MS (ESI) m/z 403 (M⁺+H).

20

Example 4404-amino-5-(3-bromophenyl)-7-(4-morpholinylbenzenesulfonyl)pyrido[2,3-d]pyrimidineStep a 3-acetyl-6-morpholinylbenzenesulphonamide

25 A solution of 4-acetylbenzenesulfonyl chloride in CH₂Cl₂ at -78° is treated with 2 equivalents of morpholine. The mixture is stirred at -78° for 1 hour and then warmed to rt and stirred for 2 additional hours. After this time, the mixture is diluted with EtOAc and is washed with water and brine. The solution is dried (Na₂SO₄) and concentrated in vacuo to afford the desired 3-acetyl-6-morpholinylbenzenesulphonamide.

Step b 2-amino-3-cyano-4-(3-bromophenyl)-6-(6-morpholinylbenzenesulphonamide)pyridine

3-acetyl-6-morpholinylbenzenesulphonamide is then cyclized as described in example 244, using dicyanostyrene derived from 3-bromobenzaldehyde, to the desired 2-amino-3-cyano-4-(3-bromophenyl)-6-(6-morpholinylbenzenesulphonamide)pyridine

The material prepared in step b is converted to the title compound by cyclization with trisformamide using conditions described in Example 370.

¹H NMR (300 MHz, d₆-DMSO) δ 8.62 (s, 1H), 8.60 (d, 2H), 8.05 (s, 1H), 7.89-7.92 (m, 3H), 7.81 (dt, 1H), 7.53-7.63 (m, 2H), 3.65 (m, 4H), 2.94 (m, 4H);

10 MS (ESI) m/z 526/528 (M⁺H, ⁷⁹Br/⁸¹Br).

Example 441

4-amino-5-(3-bromophenyl)-7-(4-N-1,4-dioxa-8-azaspiro[4.5]decan-8-ylbenzenesulphonamide)pyrido[2,3-d]pyrimidine

15 Prepared as described for Example 440 except substituting 1,4-dioxa-8-azaspiro[4.5]decan for morpholine in step a.

¹H NMR (300 MHz, d₆-DMSO) δ 8.62 (s, 1H), 8.58 (d, 2H), 8.05 (s, 1H), 7.91-7.93 (m, 3H), 7.80 (dt, 1H), 7.53-7.63 (m, 2H), 3.80 (s, 4H), 3.06 (m, 4H), 1.69 (m, 4H);
MS (ESI) m/z 582/584 (M⁺H, ⁷⁹Br/⁸¹Br).

20

Example 442

4-amino-5-(3-bromophenyl)-7-(4-N-cyclopropylbenzenesulphonamide)pyrido[2,3-d]pyrimidine

25 Prepared as described for Example 440 except substituting n-cyclopropylamine for morpholine in step a.

IR (KBr pellet) ν_{max} 3478, 3301, 3059, 2847, 2761, 2664, 1730, 1696, 1642, 1579, 1567, 1486, 1349, 1327, 1156, 1094, 887, 844, 828, 798 cm⁻¹;
MS (ESI) 496/498 (M⁺H, ⁷⁹Br/⁸¹Br).

30

Example 443

4-amino-5-(3-bromophenyl)-7-(4-piperidinebenzenesulfonamide)pyrido[2,3-d]pyrimidine

Prepared as described for Example 440 except substituting piperidine for morpholine in step a

5 ^1H NMR (300 MHz, d_6 -DMSO) δ 8.61 (s, 1H), 8.57 (d, 2H), 8.02 (s, 1H), 7.88-7.90 (m, 3H), 7.80 (dt, 1H), 7.53-7.62 (m, 2H), 2.95 (m, 4H), 1.56 (m, 4H), 1.38 (m, 2H);
MS (ESI) 524/526 (M^++H , $^{79}\text{Br}/^{81}\text{Br}$).

Example 444

10 4-amino-5-(3-bromophenyl)-7-(4-(4-cyanopiperidine)benzenesulfonamide)pyrido[2,3-d]pyrimidine

Prepared as described for Example 440 except substituting 4-cyanopiperidine (prepared in Ex. 436) for morpholine in step a.

15 ^1H NMR (300 MHz, d_6 -DMSO) δ 8.62 (s, 1H), 8.60 (d, 2H), 8.05 (s, 1H), 7.93 (s, 1H), 7.90 (m, 2H), 7.81 (dt, 1H), 7.53-7.63 (m, 2H), 3.24 (m, 2H), 2.94 (m, 1H), 2.80 (m, 2H),
1.95 (m, 2H), 1.77 (m, 2H);
MS (ESI) 549/551 (M^++H , $^{79}\text{Br}/^{81}\text{Br}$).

Example 445

20 4-amino-5-(3-bromophenyl)-7-(4-N-cyclopropylmethylbenzenesulfonamide)pyrido[2,3-d]pyrimidine

Prepared as described for Example 440 except substituting cyclopropylmethylamine for morpholine in step a.

25 ^1H NMR (300 MHz, d_6 -DMSO) δ 8.61 (s, 1H), 8.52 (d, 2H), 8.01 (d, 1H), 7.96 (d, 2H), 7.79-7.90 (m, 3H), 7.56 (m, 2H), 2.73 (m, 2H), 0.81 (m, 1H), 0.34 (m, 2H), 0.09 (m, 2H);
MS (ESI) m/z 510/512 (M^++H , $^{79}\text{Br}/^{81}\text{Br}$).

Example 446

26 4-amino-5-(3-bromophenyl)-7-(4-N,N-dimethylaminobenzenesulfonamide)pyrido[2,3-d]pyrimidine

Prepared as described for Example 440 except substituting dimethylamine for morpholine in step a.

¹H NMR (300 MHz, d₆-DMSO) δ 8.62 (s, 1H), 8.59 (d, 2H), 8.04 (s, 1H), 7.90-7.93 (m, 3H), 7.81 (dt, 1H), 7.53-7.63 (m, 2H), 2.67 (s, 6H);

5 MS (ESI) m/z 484/486 (M⁺+H, ⁷⁹Br/⁸¹Br).

Example 447

4-amino-5-(3-bromophenyl)-7-(4-N-(S)-2-

hydroxymethylpyrrolidinebenzenesulfonamide)pyrido[2,3-d]pyrimidine

10 Prepared as described for Example 440 except substituting (S-(-)-2-hydroxymethylpyrrolidine for morpholine in step a.

¹H NMR (300 MHz, d₆-DMSO) δ 8.61 (s, 1H), 8.56 (d, 2H), 8.03 (s, 1H), 7.99 (d, 2H), 7.90 (m, 1H), 7.81 (dt, 1H), 7.53-7.62 (m, 2H), 4.87 (t, 1H), 3.57 (m, 2H), 3.12 (m, 2H), 1.79 (m, 2H), 1.44 (m, 2H);

15 MS (ESI) m/z 540/542 (M⁺+H, ⁷⁹Br/⁸¹Br).

Example 448

4-amino-5-(3-bromophenyl)-7-(4-(4-hydroxypiperidine)benzenesulfonamide)pyrido[2,3-d]pyrimidine

20 Prepared as described for Example 440 except substituting 4-hydroxypiperidine for morpholine in step a.

¹H NMR (d₆-DMSO) δ 8.62 (s, 1H), 8.59 (d, 2H), 8.04 (s, 1H), 7.90-7.94 (m, 3H), 7.81 (dt, 1H), 7.52-7.63 (m, 2H), 4.86 (m, 1H), 3.06 (m, 4H), 1.91 (m, 2H), 1.69 (m, 2H);
MS (ESI) m/z 540/542 (M⁺+H, ⁷⁹Br/⁸¹Br).

25

Example 449

4-amino-5-(3-bromophenyl)-7-(4-(cis-3,5-dimethylmorpholinyl)benzenesulfonamide)pyrido[2,3-d]pyrimidine

Prepared as described for Example 440 except substituting cis-2,6-dimethylmorpholine for morpholine in step a.

¹H NMR (300 MHz, d₆-DMSO) δ 8.62 (s, 1H), 8.59 (d, 2H), 8.04 (s, 1H), 7.90 (m, 3 H), 7.80 (dt, 1H), 7.52-7.61 (m, 2H), 3.53-3.66 (m, 4H), 1.89 (m, 2H), 1.05 (d, 6H);
MS (ESI) m/z 554/556 (M⁺+H, ⁷⁹Br/⁸¹Br).

5

Example 4504-amino-5-(3-bromophenyl)-7-(3-fluoro-4-thiomorpholinylphenyl)pyrido[2,3-d]pyrimidine

Prepared as described for Example 370 using steps a and b except substituting 3-fluoro-4-thiomorpholinylacetophenone for 5-acetyl-2-chloropyridine in step a which was 10 prepared as follows 3',4'-difluoroacetophenone and thiomorpholine are stirred in DMSO at 100° for 12 hours. The mixture is cooled and quenched with water. The resulting beige solid, 3'-fluoro-4'-thiomorpholino-acetophenone, was collected by filtration and washed with water.

¹H NMR (300 MHz, d₆-DMSO) δ 8.55 (s, 1H), 8.11 (m, 1H), 7.91 (s, 1H), 7.86 (m, 1H), 15 7.78 (dt, 1H), 7.55 (m, 2H), 7.19 (t, 1H), 3.41 (m, 4H), 2.77 (m, 4H);
MS (ESI) m/z 496/498 (M⁺+H, ⁷⁹Br/⁸¹Br).

Example 4514-amino-5-(4-fluorophenyl)-7-(6-(thiomorpholinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine

20 Prepared as described in Example 370 except substituting thiomorpholine for 4-methoxypiperidine component and dicyanostyrene derived from 4-fluorobenzaldehyde for the 3-bromo derivative.

¹H NMR (300 MHz, d₆-DMSO) δ 9.06 (d, 1H), 8.52 (s, 1H), 8.44 (dd, 1H), 7.82 (s, 1H), 7.64 (m, 2H), 7.44 (m, 2H), 7.01 (d, 1H), 4.03 (m, 4H), 2.65 (m, 4H);
25 MS (ESI) m/z 419 (M⁺+H).

Example 4524-amino-5-(4-fluorophenyl)-7-(6-(4,4-dioxothiomorpholinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine

Prepared by substituting Example 451 for Example 331 as described in Example 332.

¹H NMR (300 MHz, d₆-DMSO) δ 9.10 (d, 1H), 8.53 (s, 1H), 8.51 (dd, 1H), 7.85 (s, 1H), 7.65 (m, 2H), 7.44 (m, 2H), 7.18 (d, 1H), 4.18 (m, 4H), 3.18 (m, 4H);

5 MS (ESI) m/z 451 (M⁺+H).

Example 453

4-methoxy-5-(3-bromophenyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine

Step a 4-hydroxy-5-(3-bromophenyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine

10 Example 134 was dissolved in 10:1 acetic acid : water. The mixture was heated to reflux for 1 day and cooled. The desired product was collected by filtration.

15 The 4-hydroxy-5-(3-bromophenyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine was treated with K₂CO₃ (5 eq) and 18-crown-6 (7 eq) in DMF at rt. After 1 hour, methyl iodide (30 eq) added, and the reaction continued to stir at rt. After 3 hours, the reaction was quenched with water, and the resulting solid was collected by filtration and purified by chromatography to afford the the title compound.

20 ¹H NMR (300 MHz, d₆-DMSO) δ 9.07 (d, 1H), 8.60 (s, 1H), 8.45 (dd, 1H), 7.83 (s, 1H), 7.60 (m, 2H), 7.39 (m, 2H), 6.98 (d, 1H), 3.61-3.73 (m, 8H), 3.38 (s, 3H); MS (ESI) m/z 478/480 (M⁺+H, ⁷⁹Br/⁸¹Br).

Example 454

4-amino-5-(3-bromophenyl)-7-(4-(4-dioxa-8-azaspiro[4.5]decan-8-

y]carboxamide)phenyl)pyrido[2,3-d]pyrimidine

25 step a 4-acetylbenzoylchloride

4-Acetylbenzoic acid is stirred with thionyl chloride at reflux for 90 min. The solution is cooled to roomtemperature, and the thionyl chloride is removed under reduced pressure. Residual SOCl₂ is removed by evaporation with CH₂Cl₂, and the remaining yellow residue is used without furthur purification.

30

Step b 4-(4',4'-ethylenedioxypiperidinyl)acetophenone

4-acetylbenzoylchloride prepared in step a is dissolved in CH₂Cl₂ and treated with 3 eq. of 4,4-ethylenedioxypiperidine. The reaction mixture is stirred overnight at rt and is then washed with water and brine. The solution is dried (Na₂SO₄) and concentrated in 5 vacuo to afford the desired amide.

Step c

Example 454 was prepared as described for steps a and b of Example 370, substituting the 4-(4',4'-ethylenedioxypiperidinyl)acetophenone prepared above for the 5-10 acetyl-2-chloropyridine in step a. Substituting the 4-(4',4'-ethylenedioxypiperidinyl)acetophenone prepared in step b for the 5 acetyl .
¹H NMR (300 MHz, d₆-DMSO) δ 8.59 (s, 1H), 8.39 (d, 2H), 7.97 (s, 1H), 7.89 (m, 1H), 7.80 (dt, 1H), 7.52-7.60 (m, 4H), 3.92 (s, 4H), 3.70 (m, 2H), 3.40 (m, 2H), 1.68 (m, 4H); MS (ESI) m/z 548/548 (M⁺+H, ⁷⁹Br⁸¹Br).

15

Example 455**4-amino-5-(3-bromophenyl)-7-(4-(N-cyclopropylcarboxamide)phenyl)pyrido[2,3-d]pyrimidine**

Prepared as described for Example 454 except substituting cyclopropyl amine for 20 4,4-ethylenedioxypiperidine.
¹H NMR (300 MHz, d₆-DMSO) δ 8.60-8.62 (m, 2H), 8.42 (d, 2H), 7.99 (d, 1H), 7.98 (d, 1H), 7.52-7.62 (m, 2H), 2.89 (m, 1H), 0.67-0.75 (m, 2H), 0.58-0.63 (m, 2H); MS (ESI) m/z 460/462 (M⁺+H, ⁷⁹Br⁸¹Br).

25

Example 456**4-amino-5-(3-bromophenyl)-7-(4-(morpholinylcarboxamide)phenyl)pyrido[2,3-d]pyrimidine**

Prepared as described for Example 454 except substituting morpholine for 4,4-ethylenedioxypiperidine.

¹H NMR (300 MHz, d₆-DMSO) δ 8.74 (s, 1H), 8.41 (d, 2H), 7.98 (s, 1H), 7.89 (m, 1H), 7.80 (dt, 1H), 7.52-7.61 (m, 4H), 3.52-3.71 (m, 8H);
 MS (ESI) m/z 490/492 (M⁺+H, ⁷⁹Br/⁸¹Br).

5

Example 4574-amino-5-(3-bromophenyl)-7-(6-N-cyclopropylamino-3-pyridyl)pyrido[2,3-d]pyrimidine

Prepared as described for Example 370 except substituting cyclopropyl amine for 4-hydroxypiperidine.

¹H NMR (300 MHz, d₆-DMSO) δ 8.99 (d, 1H), 8.52 (s, 1H), 8.40 (dd, 1H), 7.83 (m, 1H),
 10 7.76-7.80 (m, 2H), 7.51-7.58 (m, 2H), 7.40 (d, 1H), 6.73 (d, 1H), 2.62 (m, 1H), 0.76 (m, 2H), 0.48 (m, 2H);
 MS (ESI) m/z 433/435 (M⁺+H, ⁷⁹Br/⁸¹Br).

Example 45815 4-amino-5-(3-bromophenyl)-7-(4-(4-hydroxypiperidinylcarboxamide)phenyl)pyrido[2,3-d]pyrimidine

Prepared as described for Example 454 except substituting 4-hydroxypiperidine for 4,4-ethylenedioxypiperidine.

¹H NMR (300 MHz, d₆-DMSO) δ 8.59 (s, 1H), 8.40 (d, 2H), 8.25 (s, 1H), 7.97 (s, 1H),
 20 7.89 (t, 1H), 7.79 (dt, 1H), 7.56 (m, 3H), 5.06 (m, 1H), 3.96 (m, 2H), 3.48 (m, 2H), 1.93
 (m, 2H), 1.64 (m, 2H);
 MS (ESI) m/z 504/506 (M⁺+H, ⁷⁹Br/⁸¹Br).

Example 45925 4-amino-5-(3-bromophenyl)-7-(6-(S)-hydroxymethylpyrrolidinyl-3-pyridazinyl)pyrido[2,3-d]pyrimidine

Prepared as described for Example 367 except substituting (S)-(+)-2-hydroxymethylpyrrolidine for (1S,4S)-2-aza-5-oxa-bicyclo[2.2.1]heptane

¹H NMR (300 MHz, d₆-DMSO) δ 8.58 (s, 1H), 8.38 (d, 1H), 8.26 (s, 1H), 7.84 (m, 1H), 7.81 (dt, 1H), 7.57 (2 overlapping m, 2H), 7.16 (br d, 1H), 4.91 (t, 1H), 3.63 (m, 2H), 3.44 (m, 2H), 2.05 (m, 4H);
MS (ESI) m/z 478/480 (M⁺+H, ⁷⁹Br/⁸¹Br).

5

Example 460

4-amino-5-(3-bromophenyl)-7-(6-(4-(2-ethoxyethoxy)piperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine

Prepared as described for Example 370 except substituting 4-(2-ethoxyethoxy)piperidine for 4-methoxypiperidine, which was prepared as follows. 4-Hydroxypiperidine is treated with 1 eq. of Boc₂O in CH₂Cl₂ and stirred at rt for 5 min. The solution is then washed with water and brine, dried over Na₂SO₄, and concentrated in vacuo. The protected species is then dissolved in DMF and treated with 7 eq. of NaH. The mixture is stirred for 5 min, then 2-ethoxy-1-chloroethane (2 eq) is added, and the reaction is stirred at rt overnight. After this time, it is quenched with water and extracted with 2:1 ether-hexanes. The organic solution is dried (Na₂SO₄) and concentrated in vacuo. The oil thus obtained is finally stirred in 4M HCl-dioxane for 30 minutes. The solvent was removed in vacuo, then the residue was basified with 50% aq. NaOH solution and extracted with ether. Drying (Na₂SO₄) of the extracts, followed by removal of the solvent in vacuo, afforded the desired 4-alkoxy-piperidine.

¹H NMR (300 MHz, d₆-DMSO) δ 9.05 (d, 1H), 8.52 (s, 1H), 8.43 (dd, 1H), 7.85 (m, 2H), 7.78 (dt, 1H), 7.53 (m, 2H), 6.99 (d, 1H), 4.07 (m, 2H), 3.56 (m, 2H), 3.48 (m, 2H), 3.45 (q, 2H), 3.29 (m, 2H), 3.27 (m, 1H), 1.92 (m, 2H), 1.45 (m, 2H), 1.10 (t, 3H);
MS (ESI) m/z 549/551 (M⁺+H, ⁷⁹Br/⁸¹Br).

25

Example 461

4-amino-5-(3-bromophenyl)-7-(6-hexahydropyrimidine)-3-pyridyl)pyrido[2,3-d]pyrimidine

Prepared as described for Example 370 except substituting hexahydropyrimidine for 4-methoxypiperidine, which was prepared according to Shustov, et al Tetrahedron 1985, 41, 5719.

5 ^1H NMR (300 MHz, d_6 -DMSO) δ 9.23 (d, 1H), 8.89 (s, 1H), 8.58 (dd, 1H), 8.21 (s, 1H), 7.95 (m, 1H), 7.83 (m, 1H), 7.61 (m, 2H), 7.29 (d, 1H), 5.13 (m, 1H), 3.91 (m, 2H), 3.69 (m, 2H), 3.32 (m, 2H), 1.83 (m, 2H); MS (ESI) m/z 462/464 ($M^+ + \text{H}$, $^{79}\text{Br}^{81}\text{Br}$).

Example 462

10 4-amino-5-(4,4-difluorocyclohexyl)-7-(6-(1,4-dioxa-8-azaspiro[4.5]decan-8-yl)-3-pyridyl)pyrido[2,3-d]pyrimidine

Prepared as described for Example 370 except substituting 4,4-difluorocyclohexylcarboxaldehyde for 3-bromobenzaldehyde and 4,4-ethylenedioxypiperidine for for 4-methoxypiperidine. The 4,4-difluorocyclohexylcarboxaldehyde was prepared as follows: 4-Oxo-cyclohexanecarboxylic acid ethyl ester was stirred with 10 eq of (diethylamino)sulfur trifluoride in benzene at rt for 24 hours. The mixture was diluted with ether and was quenched carefully with saturated NaHCO_3 solution. The organic solution was separated, washed with brine, and concentrated in vacuo to afford 4,4-difluoro-cyclohexanecarboxylic acid ethyl ester. This material was treated with 1 eq. of DIBAL-H in dry ether at -78° to afford, after workup, 4,4-difluoro-cyclohexanecarboxaldehyde.

20 ^1H NMR (300 MHz, d_6 -DMSO) δ 9.13 (d, 1H), 8.79 (s, 1H), 8.44 (dd, 1H), 8.06 (s, 1H), 7.10 (d, 1H), 3.94 (s, 4H), 3.82 (m, 4H), 1.70 (m, 4H); MS (ESI) m/z 483 ($M^+ + \text{H}$).

25 Example 463

4-amino-5-(3-bromophenyl)-7-(6-(R)-2-ethoxyethoxypyrrolidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine

Prepared as described for Example 370 except substituting (S??)-2-ethoxyethoxypyrrolidine for for 4-methoxypiperidine. (R)-2-ethoxyethoxypyrrolidinyl was 30 prepared as follows:

(R)-(+)-3-Pyrrolidinol is treated with 1 eq. of Boc_2O in CH_2Cl_2 and stirred at rt for 5 min. The solution is then washed with water and brine, dried over Na_2SO_4 , and concentrated in vacuo. The protected species is then dissolved in DMF and treated with 7 eq. of NaH. The mixture is stirred for 5 min, then 2-ethoxy-1-chloroethane (2 eq) is added, and the reaction is stirred at rt overnight. After this time, it is quenched with water and extracted with 2:1 ether-hexanes. The organic solution is dried (Na_2SO_4) and concentrated in vacuo. The oil thus obtained is finally stirred in 4M HCl-dioxane for 30 minutes. The solvent was removed in vacuo, then the residue was basified with 50% aq. NaOH solution and extracted with ether. Drying (Na_2SO_4) of the extracts, followed by removal of the solvent in vacuo, afforded the 3-alkoxy-pyrrolidine derivative.

10 ^1H NMR (300 MHz, d_6 -DMSO) δ 9.06 (d, 1H), 8.52 (s, 1H), 8.44 (dd, 1H), 7.84 (m, 2H), 7.79 (dt, 1H), 7.56 (2 overlapping m, 2H), 6.62 (br d, 1H), 4.24 (m, 1H), 3.58 (m, 4H), 3.48 (m, 4H), 3.42 (q, 2H), 2.10 (m, 2H), 1.09 (t, 3H); MS (ESI) m/z 535/537 ($\text{M}^+ + \text{H}$, $^{79}\text{Br}/^{81}\text{Br}$).

15

Example 464

4-amino-5-(3-bromophenyl)-7-(6-(cis-3,4-dihydroxypyrolidiny)-3-pyridyl)pyrido[2,3-d]pyrimidine

Was prepared from Example 603 by treatment with 0.1 eq. OsO_4 and 1.2 eq. NMO in 10% MeOH- CH_2Cl_2 , and the mixture was refluxed for 13 hours and was then quenched with water and filtered. The solid thus obtained was purified by recrystallization to afford the title compound.

20 ^1H NMR (300 MHz, d_6 -DMSO) δ 9.05 (d, 1H), 8.52 (s, 1H), 8.44 (dd, 1H), 7.85-7.77 (m, 3H), 7.58-7.5 (m, 2H), 6.58 (d, 1H), 5.0 (d, 2H), 4.17 (m, 2H), 3.6 (m, 2H).

25 MS m/z 480 ($\text{M}^+ + \text{H}$)

Example 465

4-amino-5-(3-bromophenyl)-7-(6-((3aR,6aS)-2-oxo-tetrahydro-3aH-[1,3]dioxolo[4,5-c]pyrrol-5-yl)-3-pyridyl)pyrido[2,3-d]pyrimidine

Example 464 was stirred with 5 eq. of carbonyl diimidazole and 12 eq. of imidazole in DMSO at 100° for 12 hours. The solution was then cooled, quenched with water, and the resulting solid was collected by filtration and washed with water. Purification by chromatography afforded the title compound.

5 ^1H NMR (300 MHz, d_6 -DMSO) δ 9.10 (d, 1H), 8.54 (s, 1H), 8.51 (dd, 1H), 7.87 (m, 2H), 7.78 (dt, 1H), 7.54 (m, 2H), 6.91 (d, 1H), 5.48 (m, 2H), 4.18 (d, 2H), 3.48 (m, 2H);
MS (ESI) m/z 505/507 ($M^++\text{H}$, $^{79}\text{Br}/^{81}\text{Br}$).

Example 466

10 4-amino-5-(3-bromophenyl)-7-(6-(*cis*-2,3-dihydroxypyrrolidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine

Prepared as described for Example 370 except substituting pyrrolidine for 4-methoxypiperidine and subsequent oxidation of this material by the following procedure: treatment with 0.1 eq. OsO_4 and 1.2 eq. NMO in 10% $\text{MeOH}-\text{CH}_2\text{Cl}_2$ containing a few 15 drops of glacial acetic acid. The mixture was refluxed for 13 hours and was then quenched with water and filtered. The solid thus obtained was purified by recrystallization to afford the title compound.
 ^1H NMR (300 MHz, d_6 -DMSO) δ 8.93 (s, 1H), 8.47 (s, 1H), 8.31 (d, 1H), 7.92 (t, 1H), 7.83 (dt, 1H), 7.59 (m, 2H), 7.20 (d, 1H), 4.23 (m, 2H), 3.55 (m, 4H);
20 MS (ESI) m/z 480/482 ($M^++\text{H}$, $^{79}\text{Br}/^{81}\text{Br}$).

Example 467

4-amino-5-(3-bromophenyl)-7-(6-(S,R-2-hydroxymethyl-4-hydroxypyrrolidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine

25 Prepared as described for Example 370 except substituting (S,R)-2-hydroxymethyl-4-hydroxypyrrolidine for 4-methoxypiperidine, which was prepared as follows: N-Boc-hydroxyproline was treated with $\text{BH}_3\text{-SMe}_2$ (4 eq) in ether at roomtemperature. After 16 hours, the reaction was quenched with water and K_2CO_3 and was extracted with EtOAc . The combined extracts were dried and concentrated in vacuo 30 to afford N-Boc-hydroxyprolinol. The Boc group was then removed (HCl-dioxane, rt).

¹H NMR (300 MHz, d₆-DMSO) δ 9.05 (d, 1H), 8.52 (s, 1H), 8.42 (dd, 1H), 7.82 (m, 2H), 7.78 (dt, 1H), 7.54 (m, 2H), 6.66 (d, 1H), 5.02 (d, 1H), 4.95 (t, 1H), 4.47 (m, 1H), 4.23 (m, 1H), 3.46-3.66 (m, 4H), 2.16 (m, 1H), 1.96 (m, 1H); MS (ESI) m/z 493/495 (M⁺+H, ⁷⁹Br/⁸¹Br).

5

Example 468

4-amino-5-(3-bromophenyl)-7-(6-(R-2-hydroxymethyl-4-pyrrolidinyl)-3-pyridazinyl)pyrido[2.3-d]pyrimidine

Prepared as described for Example 367 except substituting R-2-hydroxymethylpyrrolidine for (1S,4S)-2-aza-5-oxa-bicyclo[2.2.1]heptane
¹H NMR (300 MHz, d₆-DMSO) δ 8.58 (s, 1H), 8.38 (d, 1H), 8.26 (s, 1H), 7.84 (m, 1H), 7.80 (dt, 1H), 7.56 (2 overlapping m, 2H), 7.16 (d, 1H), 4.89 (t, 1H), 4.23 (br, 1H), 3.62 (m, 2H), 3.45 (m, 2H), 2.05 (m, 4H); MS (ESI) m/z 478/480 (M⁺+H, ⁷⁹Br/⁸¹Br).

15

Example 469

4-amino-5-(3-bromophenyl)-7-(6-(1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptan-5-yl)-3-pyridyl)pyrido[2.3-d]pyrimidine

Prepared as described for Example 370 except substituting (1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane for 4-methoxypiperidinc, which was prepared according to Portoghesi, et al. J. Med. Chem. 1971, 14, 288
¹H NMR (300 MHz, d₆-DMSO) δ 9.05 (d, 1H), 8.52 (s, 1H), 8.43 (dd, 1H), 7.82 (m, 2H), 7.78 (dt, 1H), 7.57 (m, 2H), 6.67 (m, 1H), 5.01 (s, 1H), 4.71 (s, 1H), 3.82 (dd, 1H), 3.68 (d, 1H), 3.54 (dd, 1H), 3.38 (d, 1H), 1.93 (m, 2H); MS (ESI) m/z 475/477 (M⁺+H, ⁷⁹Br/⁸¹Br).

25

Example 470

4-amino-5-(3-bromophenyl)-7-(6-(2-imidazolidone-1-yl)-3-pyridyl)pyrido[2.3-d]pyrimidine

Prepared as described for Example 370 except substituting 1,2-ethanediamine for 4-methoxypiperidine and the resulting crude product was stirred in DMSO with carbonyl

diimidazole (4.7 eq) and imidazole (9 eq) at 100° for 16 hours. Solution quenched with water, then the solvent was removed by lyophilization. Chromatography of the residue afforded the title compound.

IR (KBr pellet) ν_{max} 3363, 3201, 3122, 3049, 2941, 1734, 1645, 1611, 1566, 1484, 1381, 5 1270, 1162, 1058, 808, 781, 767 cm^{-1} ;
MS (ESI) 462/464 (M^++H , $^{79}\text{Br}/^{81}\text{Br}$).

Example 472

4-amino-5-(1,1-dimethyl-3-butenyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine

10 A mixture of 7.6 mmol of 2,2-dimethyl-4-pentenal (Aldrich Chemical Co.), 24.4 mmol of 1-morpholino-5-acetylpyridine, 7.6 mmol of malononitrile, and 29 mmol of ammonium acetate in ethylene dichloride was heated at 120 °C in a sealed tube for 16 hours. The reaction was cooled, poured into dichloromethane, and washed with water. The organic phase was dried over Na_2SO_4 , concentrated in vacuo, and purified by flash 15 chromatography, eluting with ethyl acetate/dichloromethane to give the intermediate product pyridine.

A mixture of 1.7 mmol of this intermediate pyridine, and 45 mg of ammonium sulfate was heated in 10 mL of triethyl orthoformate at 140 °C in a sealed tube for one hour. After cooling, the reaction was poured into 40 mL of 2-M ammonia in ethanol with 20 stirring. After 24 hours, 300 mL of hexane was added, and the solid collected by filtration to give the intermediate amidine. A mixture of 0.87 mmol of this intermediate amidine and 3 mmol of potassium t-butoxide in 10 mL of dioxane was heated at 135 °C in a sealed tube for 16 hours. After cooling, the reaction was poured into dichloromethane, washed with water, and dried over sodium sulfate. The residue was purified by flash 25 chromatography, eluting with methanol/dichloromethane, to give the title compound as a yellow glass.

CHN analysis calculated for $\text{C}_{22}\text{H}_{36}\text{N}_6\text{O}$ (0.5 Methanol) C 66.48, H 6.94, N 20.67; found: C 66.18, H 6.83, N 20.65.

MS (FAB) calc. for $\text{C}_{22}\text{H}_{37}\text{N}_6\text{O}$: 391.2246; found: 391.2238.

30 IR 3417, 3340, 2965, 2853, 1603, 1584, 1563, 1533, 1241 cm^{-1} .

Example 4734-amino-5-(3-bromophenyl)-7-(6-(2,4-dioxo-(1H,3H)-quinazolin-3-yl)-3-pyridyl)pyrido[2,3-d]pyrimidine

5 A solution of 4-aminoacetophenone and triethylamine in toluene at -78 °C was treated with phosgene, warmed to ambient temperature and concentrated under reduced pressure to give 4-isocyanateacetophenone. This product was reacted with ethyl 2-aminobenzoate in refluxing THF for 16 hours, cooled and treated with 1M potassium tert-butoxide to give after silica gel purification 3-(4-acetylphenyl)-2,4(1H,3H)-10 quinazolinedione. Using the procedure in Example 244c except substituting 2,4(1H,3H)-quinazolinedione for N-methyl-5-acetylindoline gave the title compound.

15 MS (APCI +) m/z 537 (M+H)⁺;
¹H NMR (300 MHz, DMSO-d₆) δ 8.59 (s, 1H), 8.35 (m, 2H), 7.97 (s, 1H), 7.91 (t, 1H), 7.78 (m, 1H), 7.71 (dd, 1H), 7.63 (m, 1H), 7.55 (t, 1H), 7.35-7.24 (m, 3H), 6.92 (d, 1H), 15 6.72 (dt, 1H).

Example 4744-amino-5-(3-bromophenyl)-7-(6-carboxamide-3-pyridazinyl)pyrido[2,3-d]pyrimidine

Prepared as described in Example 475 except substituting ammonia for
20 morpholine.

MS (APCI +) m/z 422 (M+H)⁺;
¹H NMR (300 MHz, DMSO-d₆) δ 8.87 (d, 1H), 8.66 (s, 1H), 8.62 (bs, 1H), 8.44 (d, 1H), 8.42 (s, 1H), 8.07 (bs, 1H), 7.88 (m, 1H), 7.83 (m, 1H), 7.63 (m, 1H), 7.58 (t, 1H).

25

Example 4754-amino-5-(3-bromophenyl)-7-(6-morpholinocarboxamide-3-pyridazinyl)pyrido[2,3-d]pyrimidine

A solution of 3-chloro-6-pyridazinoyl chloride (Mourad et al.; J. Heterocycl. Chem., 29 6, (1992), pp1583-1592) and triethylamine in dichloroethane was treated with
30 morpholine to give 3-chloro-6-morpholinocarboxamide pyridazine. This intermediate was

then treated with tributyl ethoxyvinyl tin under Stille conditions to give 3-acetyl-6-morpholinocarboxamide pyridazine. Treatment of this intermediate as in Example 246 replacing 3-acetyl-6-dimethylaminopyridazine gave the title compound.

MS (APCI +) m/z 492 (M+H)⁺;

5 ¹H NMR (300 MHz, DMSO-d₆) δ 8.84 (d, 1H), 8.66 (s, 1H), 8.42 (s, 1H), 8.17 (d, 1H), 7.89 (t, 1H), 7.84 (m, 1H), 7.65 (m, 1H), 7.57 (t, 1H), 3.74 (s, 4H), 3.61 (m, 2H), 3.51 (m, 2H).

Example 476

10 4-amino-5-(3-bromophenyl)-7-(6-methoxy-3-pyridazinyl)pyrido[2,3-d]pyrimidine

Prepared as described for Example 369 replacing benzyl alcohol with methanol. Treatment with excess 4 M HCl in dioxane followed by lyophilization gave the title compound as the HCl salt.

MS (APCI +) m/z 409 (M+H)⁺;

15 ¹H NMR (300 MHz, DMSO-d₆) δ 9.90 (bs, 1H), 8.93 (s, 1H), 8.54 (d, 1H), 8.52 (s, 1H), 7.94 (t, 1H), 7.68 (m, 1H), 7.67 (m, 1H), 7.60 (d, 1H), 7.54 (d, 1H), 4.15 (s, 3H).

Example 477

20 4-amino-5-(3-bromophenyl)-7-(6-N,N-diethoxyethylamino-3-pyridazinyl)pyrido[2,3-d]pyrimidine

Prepared following the procedure in Example 246 replacing dimethylamine with bis(2-ethoxyethyl)amine. Treatment with excess 4 M HCl in dioxane followed by lyophilization gave the title compound as the di-HCl salt.

MS (APCI +) m/z 538 (M+H)⁺;

25 ¹H NMR (300 MHz, DMSO-d₆) δ 10.11 (bs, 1H), 8.89 (s, 1H), 8.40 (s, 1H), 8.26 (d, 1H), 7.89 (m, 1H), 7.81 (d, 1H), 7.64 (d, 1H), 7.58-7.46 (m, 3H), 3.88 (m, 4H), 3.63 (t, 4H), 3.44 (q, 4H), 1.09 (t, 6H).

Example 478

4-amino-5-(3-bromophenyl)-7-(6-(4-ethoxymethylpiperidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine

4-Hydroxymethyl piperidine was treated sequentially with di-tert-butyl dicarbonate, iodoethane, and trifluoroacetic acid to give 4-ethoxymethyl piperidine which 5 was reacted as in Example 367 replacing (1S,4S)-2-aza-5-oxa-bicyclo[2.2.1]heptane. Treatment with excess 4 M HCl in dioxane followed by lyophilization gave the title compound as the di-HCl salt.

MS (APCI +) m/z 520 (M+H)⁺;

10 ¹H NMR (300 MHz, DMSO-d₆) δ 10.08 (bs, 1H), 8.91 (s, 1H), 8.40 (s, 1H), 8.28 (d, 1H), 7.89 (s, 1H), 7.82 (d, 1H), 7.64 (d, 1H), 7.57 (t, 1H), 7.48 (bs, 1H), 4.56 (bd, 2H), 3.40 (q, 2H), 3.24 (d, 2H), 3.11 (t, 2H), 1.92 (m, 1H), 1.81 (d, 2H), 1.22 (m, 2H), 1.18 (t, 3H).

Example 479

4-amino-5-(3-bromophenyl)-7-(6-(4-(4-tetrahydropyranoyloxymethyl)piperidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine

4-Hydroxymethyl piperidine was treated sequentially with di-tert-butyl dicarbonate, methanesulfonyl chloride, sodium 4-tetrahydropyranoxide, and ethereal HCl to give 4-(4-tetrahydropyran)oxymethyl piperidine which was reacted as in Example 367 replacing (1S,4S)-2-aza-5-oxa-bicyclo[2.2.1]heptane. Treatment with excess 4 M HCl in 20 dioxane followed by lyophilization gave the title compound as the HCl salt.

MS (APCI +) m/z 576 (M+H)⁺;

¹H NMR (300 MHz, DMSO-d₆) δ 9.89 (bs, 1H), 8.88 (s, 1H), 8.44 (s, 1H), 8.24 (d, 1H), 7.89 (t, 1H), 7.81 (m, 1H), 7.64 (m, 1H), 7.57 (t, 1H), 7.50 (d, 1H), 7.31 (bs, 1H), 4.55 (bd, 2H), 3.78 (m, 2H), 3.52-3.22 (m, 5H), 3.07 (t, 2H), 1.89-1.79 (m, 5H), 1.41-1.16 (m, 4H).

25

Example 480

4-amino-5-(3-bromophenyl)-7-(6-(4-ethoxyethoxymethyl)piperidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine

4-Hydroxymethyl piperidine was treated sequentially with di-tert-butyl dicarbonate, 2-chloroethyl ethyl ether and ethereal HCl to give 4-ethoxyethoxymethyl

piperidine which was reacted as in Example 367 replacing (1S,4S)-2-aza-5-oxa-bicyclo[2.2.1]heptane. Treatment with excess 4 M HCl in dioxane followed by lyophilization gave the title compound as the HCl salt.

MS (APCI +) m/z 564 (M+H)⁺;

5 ¹H NMR (300 MHz, DMSO-d₆) δ 10.13 (bs, 1H), 8.90 (s, 1H), 8.33 (s, 1H), 8.29 (d, 1H), 7.88 (s, 1H), 7.81 (d, 1H), 7.74 (d, 1H), 7.63 (d, 1H), 7.54 (t, 1H), 7.50 (s, 1H), 4.55 (bd, 2H), 3.50-3.38 (m, 6H), 3.28 (d, 2H), 3.15 (t, 2H), 1.93 (m, 1H), 1.82 (d, 2H), 1.26 (m, 2H), 1.08 (t, 3H).

10

Example 481

4-amino-5-(3-bromophenyl)-7-(6-N-methyl-N-1,3-dioxolanemethylamino)-3-pyridazinyl)pyrido[2,3-d]pyrimidine

Prepared as described for Example 367 replacing (1S,4S)-2-aza-5-oxa-bicyclo[2.2.1]heptane with 2-methylaminomethyl-1,3-dioxolane.

15 MS (APCI +) m/z 494 (M+H)⁺;

¹H NMR (300 MHz, DMSO-d₆) δ 8.59 (s, 1H), 8.38 (d, 1H), 8.27 (s, 1H), 7.85-7.77 (m, 2H), 7.62-7.53 (m, 2H), 7.35 (d, 1H), 5.10 (t, 1H), 3.97-3.77 (m, 6H), 3.24 (s, 3H).

Example 482

20 4-amino-5-(3-bromophenyl)-7-(6-(1,4-dioxaspiro[4.5]decanyl-8-oxy)-3-pyridazinyl)pyrido[2,3-d]pyrimidine

Treatment of 1,4-dioxaspiro[4.5]decan-8-one with lithium aluminum hydride in diethyl ether provided 1,4-dioxaspiro[4.5]decan-8-ol which was subsequently treated as in Example 369 replacing benzyl alcohol to give the title compound.

25 MS (APCI +) m/z 535 (M+H)⁺;

¹H NMR (300 MHz, DMSO-d₆) δ 8.62 (s, 1H), 8.60 (d, 1H), 8.28 (s, 1H), 7.85-7.77 (m, 2H), 7.60 (m, 2H), 7.40 (d, 1H), 5.42 (m, 1H), 3.90 (s, 4H), 2.10-1.55 (m, 8H).

Example 483

4-amino-5-(3-bromophenyl)-7-(6-dihydroxymethylmethoxy-3-pyridazinyl)pyrido[2,3-d]pyrimidine

Prepared as described for Example 369 replacing benzyl alcohol with cis 1,3-O-benzylidene glycerol. Treatment with excess 4 M HCl in dioxane followed by 5 lyophilization gave the title compound as the HCl salt.
MS (APCI +) m/z 469 (M+H)⁺;
¹H NMR (300 MHz, DMSO-d₆) δ 10.05 (bs, 1H), 8.93 (s, 1H), 8.51 (d, 1H), 8.50 (s, 1H), 7.92 (s, 1H), 7.82 (d, 1H), 7.66 (d, 1H), 7.59 (t, 1H), 7.53 (d, 1H), 4.59 (dd, 2H), 4.45 (dd, 2H), 3.90 (m, 1H), 3.45 (m, 2H).

10

Example 484

4-amino-5-(3-bromophenyl)-7-(6-(3-pyridyloxy)-3-pyridazinyl)pyrido[2,3-d]pyrimidine

Prepared as described for Example 369 replacing benzyl alcohol with 3-hydroxypyridine. Treatment with excess 4 M HCl in dioxane followed by lyophilization 15 gave the title compound as the di-HCl salt.
MS (APCI +) m/z 472 (M+H)⁺;
¹H NMR (300 MHz, DMSO-d₆) δ 10.10 (bs, 1H), 8.98 (s, 1H), 8.69 (d, 1H), 8.67 (s, 1H), 8.56 (dd, 1H), 8.51 (s, 1H), 7.93-7.79 (m, 4H), 7.68-7.53 (m, 4H).

20

Example 485

4-amino-5-(3-bromophenyl)-7-(6-(4,7-epoxy-7-methyl-2,3,3A,4,5,6,7,7a-octahydro-1H-isoindolyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine

Prepared as described for Example 367 replacing (1S,4S)-2-aza-5-oxa-bicyclo[2.2.1]heptane with 4,7-epoxy-7-methyl-2,3,3A,4,5,6,7,7a-octahydro-1H-isoindole 25 hydrochloride (SALOR) and adding potassium carbonate. Treatment with excess 4 M HCl in dioxane followed by lyophilization gave the title compound as the di-HCl salt.
MS (APCI +) m/z 530 (M+H)⁺;
¹H NMR (300 MHz, DMSO-d₆) δ 10.03 (bs, 1H), 8.93 (s, 1H), 8.46 (s, 1H), 8.30 (d, 1H), 7.92 (m, 1H), 7.83 (dd, 1H), 7.67-7.52 (m, 3H), 7.26 (d, 1H), 4.33 (d, 1H), 3.95-3.32 (m, 30 4H), 2.78 (m, 1H), 2.66 (m, 1H), 1.72-1.44 (m, 4H), 1.42 (s, 3H).

Example 4864-amino-5-(3-bromophenyl)-7-(6-(4-N-ethyl-N-methoxyethyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine

5 Boc-piperidine-4-carboxylic acid was coupled with N-ethylmethoxyethylamine using standard amide formation conditions to give Boc-piperidine-4-(N-ethylmethoxyethyl) carboxamide. This material was treated with HCl and the resulting amine was reacted as in Example 367 replacing (1S,4S)-2-aza-5-oxa-bicyclo[2.2.1]heptane to give the desired product. Treatment with excess 4 M HCl in dioxane followed by 10 lyophilization gave the title compound as the di-HCl salt.

10 MS (APCI +) m/z 591 (M+H)⁺;

¹H NMR (300 MHz, DMSO-d₆) δ 10.00 (bs, 1H), 8.93 (s, 1H), 8.50 (s, 1H), 8.27 (d, 1H), 7.92 (m, 1H), 7.83 (d, 1H), 7.67-7.45 (m, 4H), 4.59 (d, 2H), 3.55-2.95 (12H), 1.80-1.52 (m, 4H), 1.05 (t, 3H).

15

Example 4874-amino-5-(3-bromophenyl)-7-(6-(4-N-methyl-N-methoxyethyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine

The title compound was prepared following the procedure of Example 486 20 replacing N-ethylmethoxyethylamine with N-methylmethoxyethylamine.

MS (APCI +) m/z 577 (M+H)⁺;

¹H NMR (300 MHz, DMSO-d₆) δ 10.07 (bs, 1), 8.91 (s, 1H), 8.45 (s, 1H), 8.28 (d, 1H), 7.90 (m, 1H), 7.82 (dd, 1H), 7.67-7.53 (m, 3H), 7.48 (bs, 1H), 4.56 (bd, 1H), 3.62-3.05 (m, 8H), 3.53 (s, 3H), 3.10 (s, 3H), 1.84-1.54 (m, 4H).

25

Example 4884-amino-5-(3-bromophenyl)-7-(6-(3,4-dimethoxymethoxypyrrolidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine

Prepared as described for Example 367 replacing (1*S*,4*S*)-2-aza-5-oxa-bicyclo[2.2.1]heptane with *cis*-3,4-bis(methoxymethoxy) pyrrolidine (Rosenberg et al.; *J Med Chem* **33**, 7 (1990) pp1962-1969).

MS (APCI +) m/z 568 (M+H)⁺;

5 ¹H NMR (300 MHz, DMSO-d₆) δ 8.58 (s, 1H), 8.40 (d, 1H), 8.26 (s, 1H), 7.85-7.76 (m, 2H), 7.62-7.50 (m, 2H), 7.12 (d, 1H), 4.72 (m, 4H), 4.37 (m, 2H), 3.80 (bm, 2H), 3.63 (bm, 2H), 3.32 (s, 6H).

Example 489

10 4-amino-5-(3-bromophenyl)-7-(6-(hexahydro-1H-furo[3,4-c]pyrrol-5-vl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine

Prepared as described for Example 367 replacing (1*S*,4*S*)-2-aza-5-azabicyclo[2.2.1]heptane with hexahydro-1H-furo[3,4-c]pyrrole (US Patent 3910950, ICI United States Inc. 1975). Treatment with excess 4 M HCl in dioxane followed by 15 lyophilization gave the title compound as the di-HCl salt.

MS (APCI +) m/z 490 (M+H)⁺;

¹H NMR (300 MHz, DMSO-d₆) δ 10.01 (bs, 1H), 8.93 (s, 1H), 8.48 (s, 1H), 8.30 (d, 1H), 7.90 (m, 1H), 7.84 (m, 1H), 7.65 (m, 1H), 7.57 (t, 1H), 7.48 (bs, 1H), 7.20 (d, 1H), 3.85 (m, 4H), 3.68-3.45 (m, 4H), 3.12 (m, 2H).

20

Example 490

4-amino-5-(3-bromophenyl)-7-(6-(hexahydro-1H-furo[3,4-c]pyrrol-5-vl)-3-pyridyl)pyrido[2,3-d]pyrimidine

Prepared as described for Example 370 replacing 4-methoxypiperidine with 25 hexahydro-1H-furo[3,4-c]pyrrole (US Patent 3910950, ICI United States Inc. 1975). Treatment with excess 4 M HCl in dioxane followed by lyophilization gave the title compound as the di-HCl salt.

MS (APCI +) m/z 489 (M+H)⁺;

¹H NMR (300 MHz, DMSO-d₆) δ 9.98 (bs, 1H), 9.03 (d, 1H), 8.88 (s, 1H), 8.67 (dd, 1H), 8.22 (s, 1H), 7.95 (m, 1H), 7.82 (dd, 1H), 7.64 (d, 1H), 7.55 (t, 1H), 7.34 (bs, 1H), 7.03 (d, 1H), 3.90-3.11 (m, 10H).

5

Example 491

4-amino-5-(3-bromophenyl)-7-(6-(trans-3-hydroxy-4-methylpyrrolidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine

Prepared as described for Example 367 replacing (1S,4S)-2-aza-5-oxa-10
bicyclo[2.2.1]heptane with (anti)-3-hydroxy-4-methylpyrrolidine hydrochloride (PCT
10 Int.Appl. (1992) WO,210191) and adding potassium carbonate. Treatment with excess 4
M HCl in dioxane followed by lyophilization gave the title compound as the di-HCl salt.
MS (APCI +) m/z 478 (M+H)⁺;
15 ¹H NMR (300 MHz, DMSO-d₆) δ 10.06 (s, 1H), 8.93 (s, 1H), 8.42 (s, 1H), 8.35 (d, 1H),
7.91 (m, 1H), 7.84 (dd, 1H), 7.65 (dd, 1H), 7.57 (t, 1H), 7.50 (bs, 1H), 7.35 (d, 1H), 4.02
(m, 1H), 3.95-3.30 (m, 5H), 2.27 (m, 1H), 1.05 (d, 3H).

Example 492

4-amino-5-(3-bromophenyl)-7-(6-(trans-3-hydroxy-4-methylpyrrolidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine

20 Prepared as described for Example 370 replacing 4-methoxypiperidine with (anti)-
3-hydroxy-4-methylpyrrolidine hydrochloride (PCT Int.Appl. (1992) WO,210191) and
potassium carbonate. Treatment with excess 4 M HCl in dioxane followed by
lyophilization gave the title compound as the di-HCl salt.
MS (APCI +) m/z 477 (M+H)⁺;
25 ¹H NMR (300 MHz, DMSO-d₆) δ 10.12 (bs, 1H), 9.00 (d, 1H), 8.90 (s, 1H), 8.78 (dd,
1H), 8.26 (s, 1H), 7.97 (s, 1H), 7.82 (d, 1H), 7.64 (d, 1H), 7.57 (t, 1H), 7.42 (s, 1H), 7.20
(d, 1H), 4.07-3.30 (m, 6H), 2.30 (m, 1H), 1.03 (d, 3H).

Example 493

4-amino-5-(3-bromophenyl)-7-(6-(cis-3-hydroxy-4-methylpyrrolidinyl)-3-pyridinyl)pyrido[2,3-d]pyrimidine

Prepared as described for Example 367 replacing (1S,4S)-2-aza-5-oxa-
bicyclo[2.2.1]heptane with (anti)- 3-hydroxy-4-methylpyrrolidine hydrochloride (PCT
5 Int.Appl. (1992) WO₉210191) and potassium carbonate. Treatment with excess 4 M HCl
in dioxane followed by lyophilization gave the title compound as the di-HCl salt.
MS (APCI +) m/z 478 (M+H)⁺;
¹H NMR (300 MHz, DMSO-d₆) δ 10.18 (bs, 1H), 8.92 (s, 1H), 8.42 (d, 1H), 8.26 (s, 1H),
7.91 (s, 1H), 7.83 (d, 1H), 7.70-7.51 (m, 4H), 4.40-3.64 (m, 5H), 3.30 (t, 1H), 2.38 (m,
10 1H), 1.18 (d, 3H).

Example 494

4-amino-5-(3-bromophenyl)-7-(6-(cis-3-hydroxy-4-methylpyrrolidinyl)-3-pyridinyl)pyrido[2,3-d]pyrimidine

15 Prepared as described for Example 370 replacing 4-methoxypiperidine with (syn)-
3-hydroxy-4-methylpyrrolidine hydrochloride (PCT Int.Appl. (1992) WO₉210191) and
potassium carbonate. Treatment with excess 4 M HCl in dioxane followed by
lyophilization gave the title compound as the di-HCl salt.
MS (APCI +) m/z 477 (M+H)⁺;
20 ¹H NMR (300 MHz, DMSO-d₆) δ 10.08 (bs, 1H), 8.97 (d, 1H), 8.90 (s, 1H), 8.78 (dd,
1H), 8.26 (s, 1H), 7.97 (m, 1H), 7.82 (m, 1H), 7.65 (dd, 1H), 7.57 (t, 1H), 7.42 (s, 1H),
7.20 (d, 1H), 4.26 (s, 1H), 4.10-3.22 (m, 5H), 2.38 (m, 1H), 1.08 (d, 3H).

Example 495

4-amino-5-(3-bromophenyl)-7-(6-(trans-3-cyano-4-hydroxypyrrrolidinyl)-3-pyridinyl)pyrido[2,3-d]pyrimidine

Prepared as described for Example 370 replacing 4-methoxypiperidine with 3-
cyano-4-hydroxypyrrrolidine hydrochloride (Hong et al.: J Med Chem. 40, 22, (1997) pp
3584-3593) and potassium carbonate. Treatment with excess 4 M HCl in dioxane followed
30 by lyophilization gave the title compound as the di-HCl salt.

MS (ESI +) m/z 488 (M+H)⁺;

¹H NMR (300 MHz, DMSO-d₆) δ 10.03 (bs, 1H), 9.08 (d, 1H), 8.88 (s, 1H), 8.65 (t, 1H), 8.20 (s, 1H), 7.95 (s, 1H), 7.82 (d, 1H), 7.62 (d, 1H), 7.55 (t, 1H), 7.32 (d, 1H), 7.00 (d, 1H), 4.65 (m, 1H), 4.15-3.50 (m, 6H).

5

Example 496

4-amino-5-(3-bromophenyl)-7-(6-(3-hydroxy-4-tert-butylcarboxamidepyrrolidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine

The compound was isolated from the reaction mixture of Example 495. Treatment 10 with excess 4 M HCl in dioxane followed by lyophilization gave the title compound as the di-HCl salt.

MS (ESI +) m/z 562 (M+H)⁺;

¹H NMR (300 MHz, DMSO-d₆) δ 10.03 (bs, 1H), 9.05 (d, 1H), 8.52 (s, 1H), 8.44 (dd, 1H), 7.85-7.76 (m, 3H), 7.57-7.51 (m, 3H), 7.32 (s, 1H), 6.60 (d, 1H), 5.28 (d, 1H), 4.56 15 (m, 1H), 3.70-3.25 (m, 4H), 3.03 (m, 1H), 1.27 (s, 9H).

Example 497

4-amino-5-(3-bromophenyl)-7-(6-(S-2-(4-tetrahydropyranloxy)methylpyrrolidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine

20 A solution of (S)-Boc-2-pyrrolidinemethanol and triethylamine in dichloromethane at 0 °C was treated with methanesulfonyl chloride. The resulting mesylate was treated with 1.5 eq each of 4-hydroxytetrahydropyran and powdered potassium hydroxide in DMSO to afford the tetrahydropyranyl ether. Deprotection of the Boc amine with trifluoroacetic acid provided the free base pyrrolidine which was reacted 25 as in Example 367 replacing (1S,4S)-2-aza-5-oxa-bicyclo[2.2.1]heptane. Treatment with excess 4 M HCl in dioxane followed by lyophilization gave the title compound as the di-HCl salt.

MS (ESI +) m/z 562 (M+H)⁺;

¹H NMR (300 MHz, DMSO-d₆) δ 10.00 (bs, 1H), 8.93 (s, 1H), 8.49 (s, 1H), 8.30 (d, 1H), 7.91 (m, 1H), 7.84 (m, 1H), 7.64 (m, 1H), 7.58 (t, 1H), 7.49 (bs, 1H), 7.27 (bd, 1H), 4.45 (m, 1H), 3.78-3.25 (m, 9H), 2.04 (m, 4H), 1.78 (m, 2H), 1.37 (m, 2H).

5

Example 498

4-amino-5-(3-bromophenyl)-7-(6-(3-(4-tetrahydropyranyloxy)iminopyrrolidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine

Equimolar amounts of 1-N-Boc-3-pyrrolidinone and O-(tetrahydro-2H-pyran-4-yl) hydroxylamine hydrochloride (JP 07173169 Takeda Chemical Industries Ltd (1995)) were heated at reflux in 1:1 ethanol/pyridine, cooled and concentrated to give after silica gel chromatography the desired Boc protected oxime. Deprotection with trifluoroacetic acid afforded the free base pyrrolidine which was treated as in Example 367. replacing (1S,4S)-2-aza-5-oxa-bicyclo[2.2.1]heptane. Treatment with excess 4 M HCl in dioxane followed by lyophilization gave the title compound as the di-HCl salt.

15 MS (ESI +) m/z 561 (M+H)⁺; .
¹H NMR (300 MHz, DMSO-d₆) δ 10.11 (bs, 1H), 8.92 (s, 1H), 8.41 (d, 1H), 8.35 (dd, 1H), 7.90 (d, 1H), 7.83 (m, 1H), 7.65-7.33 (m, 4H), 4.38 (d, 2H), 4.25 (m, 1H), 4.10-3.72 (m, 4H), 3.44 (m, 2H), 2.93 (m, 2H), 1.93 (m, 2H), 1.55 (m, 2H).

20

Example 500

4-amino-5-(3-bromophenyl)-7-(5-bromo-2-thienyl)pyrido[2,3-d]pyrimidine

Procedure as found in Example 357 except substituting 2-acetyl-5-bromo thiophene (Lancaster) for 5-acetyl-2-morpholinylthiazole.

MS (DCI/NH₃) m/z 463/465 (M+H)⁺;

25 IR (microscope) 3473, 3299, 1580, 1557, 1073 cm⁻¹.

Example 501

4-amino-5-(3-bromophenyl)-7-(2,5-dimethyl-3-thienyl)pyrido[2,3-d]pyrimidine

Procedure as found in Example 357 except substituting 3-acetyl-2,5-dimethylthiophene (Acros) for 5-acetyl-2-morpholinylthiazole.

mp: 210-212 °C;

MS (DCI/NH₃) m/z 411/413 (M+H)⁺;

IR (microscope) 3477, 3058, 1555, 1574, 1142 cm⁻¹.

5

Example 502

4-amino-5-(3-bromophenyl)-7-(5-chloro-2-thienyl)pyrido[2,3-d]pyrimidine

Procedure as found in Example 357 except substituting 2-acetyl-5-chlorothiophene (Acros) for 5-acetyl-2-morpholinylthiazole.

mp: 264-265 °C;

10 MS (DCI/NH₃) m/z 417/419 (M+H)⁺;

IR (microscope) 3466, 3290, 1635, 1561, 1114 cm⁻¹.

Example 503

4-amino-5-(3-bromophenyl)-7-(2,4-dimethyl-5-thiazoyl)pyrido[2,3-d]pyrimidine

15 Procedure as found in Example 357 except substituting 5-acetyl-2,4-dimethylthiazole (Acros) for 5-acetyl-2-morpholinylthiazole.

mp: 254-255 °C; MS (DCI/NH₃) m/z 412/414 (M+H)⁺;

IR (microscope) 3477, 3299, 1648, 1563, 1285 cm⁻¹.

20

Example 504

4-amino-5-(3-bromophenyl)-7-(5-methyl-2-thienyl)pyrido[2,3-d]pyrimidine

Procedure as found in 357 except substituting 2-acetyl-5-methylthiophene (Lancaster) for 5-acetyl-2-morpholinylthiazole.

MS (DCI/NH₃) m/z 397/399 (M+H)⁺;

25 IR (microscope) 3294, 3218, 1618, 1581, 1065 cm⁻¹.

Example 505

4-amino-5-(3-bromophenyl)-7-(2-furanyl)pyrido[2,3-d]pyrimidine

Procedure as found in 357 except substituting 2-acetyl furan (Aldrich) for 5-acetyl-2-morpholinylthiazole. MS (DCI/NH₃) m/z 367/369 (M+H)⁺;

IR (microscope) 3485, 3110, 1642, 1563, 1008 cm^{-1} .

Example 506

4-amino-5-(3-bromophenyl)-7-(2-(1,4-dioxa-8-azaspiro[4.5]decan-8-yl)-5-thiazoyl)pyrido[2,3-d]pyrimidine

5

Procedure as found in 357 substituting 4,4-dioxyethylenepiperidine (Aldrich) for morpholine in Example 357a.

mp: >285 °C; MS (DCI/NH₃) m/z 525/527 (M+H)⁺;

IR (microscope) 3493, 3087, 1648, 1584, 1142 cm^{-1} .

10

Example 507

4-amino-5-(3-bromophenyl)-7-(3-thienyl)pyrido[2,3-d]pyrimidine

Procedure as found in Example 357 substituting 3-acetylthiophene (Aldrich) for the product from Example 357b in 357c. MS (DCI/NH₃) m/z 383/385 (M+H)⁺; IR

15 (microscope) 3473, 3100, 1638, 1561, 1288 cm^{-1} .

Example 508

4-amino-5-(3-bromophenyl)-7-(3-methyl-2-thienyl)pyrido[2,3-d]pyrimidine

Procedure as found in Example 357 substituting 2-acetyl-3-methylthiophene 20 (Lancaster) for the product from Example 357b in Example 357c. mp: 271-272 °C; MS (DCI/NH₃) m/z 397/399 (M+H)⁺; IR (microscope) 3470, 3060, 1644, 1560, 1123 cm^{-1} .

Example 509

4-amino-5-(3-bromophenyl)-7-(2-morpholinyl-4-thiazoyl)pyrido[2,3-d]pyrimidine

25 Procedure as found in Example 357 substituting the product from Example 509c for the product from 357b in 357c to give the title compound. mp: 278-282 °C; MS (DCI/NH₃) m/z 469/471 (M+H)⁺; IR (microscope) 3468, 3085, 1653, 1559, 1116 cm^{-1} .

509a: 1-Bromobutane-2,3-dione-3-oxime

2,3-butanedione (30 mL, 355 mmol; Aldrich) at 0 °C was treated with 10 drops of bromine (caution:delayed exothermic reaction). After 20 minutes, additional bromine (12.2 mL, 237 mmol) was added dropwise at such a rate as to maintain reaction temperature between 20-30 °C. Vacuum distillation (10 mmHg; fractions between 37-48 5 °C) provided 16.26 g (41%) of 1-bromo-2,3-butanedione compound as a yellow oil. A solution of 1-bromo-2,3-butanedione (16.26 g, 98.55 mmol) in water at 0 °C was treated dropwise with a solution of hydroxylamine hydrochloride (6.90 g, 99.29 mmol) and sodium carbonate (4.20 g, 39.63 mmol) in water (38 mL). After 1 hour, the reaction was extracted with dichloromethane, concentrated to one fourth the original volume, cooled 10 and filtered to provide 7.08 g (40%) of the desired compound as an unstable (freezer) white solid.

509b: 1-(2-Morpholinothiazol-5-yl)ethanoneoxime

15 A solution of known morpholine-4-carbothioic acid amide (2.66 g, 18.2 mmol; J. Het. Chem. 1987, 24, 1509) and the product from Example 509a (3.29 g, 18.3 mmol) in ethanol (5.5 mL) was heated to reflux for 2 hours. The reaction mixture was cooled to room temperature and the solid filtered, washed with ethanol and dried to provide 4.16 g (99%) of the desired compound as pink solid. MS (DCI/NH₃) m/z 228 (M+H)⁺.

20 509c: 1-(2-Morpholinothiazol-5-yl)ethanone

25 A solution of the product from Example 509b (6.00 g, 26.4 mmol) in water (250 mL), sulfuric acid (27 mL) and ethanol (26 mL) at 50 °C was treated dropwise with sodium nitrite (1.97 g, 28.5 mmol) as a solution in water (50 mL). After 2 hours, the mixture was cooled to 0 °C, neutralized with ammonium hydroxide and extracted with dichloromethane. The organic phases were concentrated and purified by silica gel chromatography (elution with 10% ethyl acetate/dichloromethane) to give 1.06 g (19%) the desired compound as a pink solid. MS (DCI/NH₃) m/z 213 (M+H)⁺.

Example 510

4-amino-5-(3-bromophenyl)-7-(2-morpholiny1-4-trifluoromethyl-5-thiazoyl)pyrido[2,3-d]pyrimidine

Procedure as found in Example 357 substituting the product from Example 510a for the product from Example 357a in Example 357b to give the title compound. mp: 277-278 °C; MS (DCI/NH₃) m/z 537/539 (M+H)⁺; IR (microscope) 3481, 3061, 1607, 1544, 1116 cm⁻¹.

step a: 2-Morpholino-4-trifluoromethylthiazole

Procedure as found in Example 509b substituting 3-bromo-1,1,1-trifluoroacetone (Aldrich) for the product from Example 509a. MS (DCI/NH₃) m/z 239 (M+H)⁺.

Example 511

4-amino-5-(3-bromophenyl)-7-(5-morpholiny1-2-thienyl)pyrido[2,3-d]pyrimidine

15 Procedure as found in 357 substituting the product from Example 511a for the product from Example 357b in Example 357c. mp: 265 °C (dec); MS (ESI) m/z 468/470 (M+H)⁺; IR (microscope) 3484, 3052, 1647, 1581, 1118 cm⁻¹.

511a: 5-Acetyl-2-morpholinothiophene

20 A solution of 5-acetyl-2-bromothiophene (8.01 g, 39.1 mmol; Aldrich) and morpholine (16 mL) was heated to 145 °C overnight. The reaction mixture was cooled and partitioned between water and dichloromethane. The organic phase was concentrated and purified by silica gel chromatography (elution with 30% hexane/ethyl acetate) to give 5.61 g (68%) of the desired compound. MS (DCI/NH₃) m/z 212 (M+H)⁺.

25

Example 512

4-amino-5-(3-bromophenyl)-7-(4-methyl-2-morpholiny1-5-thiazoyl)pyrido[2,3-d]pyrimidine

Procedure as found in Example 357 substituting the product from Example 357a for the product from Example 357a in Example 357b to provide the title compound. mp:

>280 °C; MS (DCI/NH₃) m/z 483/485 (M+H)⁺; IR (microscope) 3481, 3078, 1653, 1510, 1117 cm⁻¹.

512a: 4-Methyl-2-morpholinothiazole

5 Procedure as in Example 509b substituting chloroacetone (Aldrich) for the product from 509a. MS (DCI/NH₃) m/z 185 (M+H)⁺.

Example 513

4-amino-5-(3-bromophenyl)-7-(2,5-dichloro-3-thienyl)pyrido[2,3-d]pyrimidine

10 Procedure as found in Example 357 substituting 3-acetyl-2,5-dichlorothiophene (Aldrich) for the product from Example 357b in Example 357c to provide the title compound. mp: 258-259 °C; MS (DCI/NH₃) m/z 451/453 (M+H)⁺; IR (microscope) 3477, 3060, 1651, 1564, 1044 cm⁻¹.

15 **Example 514**

4-amino-5-(3-bromophenyl)-7-(2,5-dimethyl-3-furanyl)pyrido[2,3-d]pyrimidine

Procedure as found in Example 357 substituting 3-acetyl-2,5-dimethylfuran (Lancaster) for the product from Example 357b in Example 357c to provide the title compound. MS (DCI/NH₃) m/z 395/397 (M+H)⁺; IR (microscope) 3492, 3092, 1641, 20 1581, 1222 cm⁻¹.

Example 515

4-amino-5-(3-bromophenyl)-7-(N-methyl-2-pyrrolyl)pyrido[2,3-d]pyrimidine

25 Δ solution of the product from Example 515a (3.30 g, 9.34 mmol) and triethylorthoformate (20 mL) was treated with a catalytic amount of ammonium sulfate and heated to 100 °C for 2 hours. The reaction mixture was cooled, treated with ammonia (2 M in ethanol, 50 mL) and stirred overnight. The dark mixture was then treated with sodium methoxide (3 M in methanol, 30 mL) and heated to reflux for 3 hours. The reaction was cooled, concentrated and the residue taken up in water and neutralized with 30 10% hydrochloric acid. The aqueous phase was extracted with dichloromethane, the

organic phase concentrated and purified by silica gel chromatography (elution with 5% methanol/dichloromethane) to provide 830 mg (23%) of the title compound. MS (DCI/NH₃) m/z 380/382 (M+H)⁺; IR (microscope) 3482, 3051, 1643, 1580, 1073 cm⁻¹.

5 515a: 4-(3-Bromophenyl)-3-cyano-6-(2-(N-methylpyrrole)pyridine-2-amine

Procedure as found in Example 357c substituting 2-acetyl-1-methylpyrrole for the product from 357b.

MS (DCI/NH₃) m/z 353/355 (M+H)⁺.

10 Example 516

4-amino-5-(3-bromophenyl)-7-(2-N,N-dimethylamino-5-thiazoyl)pyrido[2,3-d]pyrimidine

Procedure as found in Example 357 substituting dimethylamine (40% in water, Aldrich) for morpholine in Example 357a. mp: >280 °C; MS (DCI/NH₃) m/z 427/429 (M+H)⁺; IR (microscope) 3455, 3054, 1636, 1503, 1035 cm⁻¹.

15 Example 517

4-amino-5-(3-bromophenyl)-7-(2-morpholinyl-5-thiazoyl)pyrido[2,3-d]pyrimidine

Procedure as found in Example 515 substituting thiomorpholine for morpholine in Example 357a to provide the title compound. MS (DCI/NH₃) m/z 485/487 (M+H)⁺; IR (microscope) 3474, 3083, 1641, 1509, 1129 cm⁻¹.

Example 518

4-amino-5-(3-bromophenyl)-7-(2-(1,1-dioxidothiomorpholinyl)-5-thiazoyl)pyrido[2,3-d]pyrimidine

25 A solution of the product from Example 517 (402 mg, 0.83 mmol) in acetic acid and acetone was treated with potassium permanganate in water until complete consumption of starting material was detected. Reaction mixture poured over ice, the solution made strongly basic with 50% sodium hydroxide. The resulting solid was filtered and purified by silica gel chromatography (elution with 5% methanol/dichloromethane) to

provide 231 mg (54%) of the title compound as a yellow solid. MS (DCI/NH₃) m/z 517/519 (M+H)⁺; IR (microscope) 3484, 3056, 1606, 1501, 1125 cm⁻¹.

Example 519

5 4-amino-5-(3-bromophenyl)-7-(1-N-methyl-2-morpholinyl-5-imidazolyl)pyrido[2,3-d]pyrimidine

Procedure as in Example 515 substituting the product from Example 519a for the product of Example 357b in Example 357c. MS (DCI/NH₃) m/z 466/468 (M+H)⁺; IR (microscope) 3479, 3089, 1646, 1587, 1118 cm⁻¹.

10

519a: 4-Acetyl-1-methyl-2-morpholinylimidazole

A solution of 5-acetyl-2-aminooxazole (7.00 g, 55.5 mmol; J. Org. Chem. 1984, 49, 566) and morpholine (20 mL) in water (14 mL) was heated to reflux overnight. The reaction was cooled to room temperature, concentrated and triturated with ethyl acetate, 15 filtered and dried to provide 3.52 g (33%) of the desired compound. A slurry of sodium hydride (60% in oil, 590 mg, 14.7 mmol) and methyl iodide (0.86 mL, 13.7 mmol) in tetrahydrofuran (20 mL) at room temperature was added a solution of 4-acetyl-2-morpholinylimidazole (2.44 g, 12.5 mmol) in dimethylformamide (13 mL) and stirring continued for 1.5 hours. Reaction quenched with ethanol, water added and extracted with 20 dichloromethane. The organic phases were combined, dried (Na₂SO₄), concentrated and the residue purified by silica gel chromatography (elution with 25% dichloromethane/ethyl acetate) to provide 1.27 g (49%) of the desired compound. MS (DCI/NH₃) m/z 210 (M+H)⁺.

25

Example 520

4-amino-5-(3-bromophenyl)-7-(2-morpholinyl-5-oxazolyl)pyrido[2,3-d]pyrimidine

Procedure as found in Example 357 substituting the product for Example 520a for the product of Example 357b in Example 357c. MS (DCI/NH₃) m/z 453/455 (M+H)⁺; IR (microscope) 3502, 3388, 1607, 1575, 1116 cm⁻¹.

30

520a: 5-Acetyl-2-morpholinooxazole

5 A solution of 2-bromo-3-oxobutyraldehyde (6.00 g, 36.4 mmol; Bull. Chem. Soc. Jpn. 1965, 38, 1158) and morpholine-4-carboxylic acid amide (9.01 g, 69.2 mmol; J. Am. Chem. Soc. 1945, 67, 1055) in acetone (40 mL) was stirred at room temperature for 1 hour then at reflux for 1 hour. The solvent removed in vacuo and the residue purified by silica gel chromatography (gradient elution with 10% ethyl acetate/dichloromethane to ethyl acetate) to provide 2.85 g (40%) of the desired compound as a yellow solid. MS (DCI/NH₃) m/z 197 (M+H)⁺.

10 Example 521**4-amino-5-(3-bromophenyl)-7-(2-N-methyl-N-methoxyethylamino-5-thiazolyl)pyrido[2,3-d]pyrimidine**

15 Procedure as found in Example 357 substituting the product from Example 521b for the product from Example 357b in Example 357c. MS (DCI/NH₃) m/z 471/473 (M+H)⁺; IR (microscope) 3472, 3051, 1645, 1519, 1090 cm⁻¹.

521a: 2-(N-methyl-N-(2-methoxyethylamino)thiazole

20 Procedure as found in Example 357a substituting (2-methoxyethyl)methylamine (TCI Japan) for morpholine. MS (DCI/NH₃) m/z 173 (M+H)⁺.

521b: 5-Acetyl-2-(N-methyl-N-(2-methoxyethylamino)thiazole

25 A solution of the product from Example 521a (4.98 g, 28.9 mmol) in tetrahydrofuran (150 mL) at -78 °C was treated with n-BuLi (2.3 M in hexanes, 15 mL) and stirring continued for 40 minutes. The light yellow solution was then treated with acetaldehyde (9.00 mL, 161 mmol), stirred for 15 minutes, quenched with saturated aqueous ammonium chloride, extracted with ethyl acetate, dried (Na₂SO₄) and concentrated. The residue was taken up in dichloromethane (150 mL) and treated with manganese dioxide (5 weight equivalents) and heated to reflux for 20 hours. The reaction mixture was cooled, filtered and concentrated to provide 4.62 g (75%) of the desired compound. MS (DCI/NH₃) m/z 215 (M+H)⁺.

Example 5224-amino-5-(3-bromophenyl)-7-(2-N-methyl-N-ethylamino-5-thiazoyl)pyrido[2,3-d]pyrimidine

5 Procedure as found in Example 357 substituting methylethyl amine (Aldrich) for (2-methoxyethyl)methylamine in Example 521a. MS (DCI/NH₃) m/z 441/443 (M+H)⁺; IR (microscope) 3493, 3041, 1655, 1524, 1133 cm⁻¹.

Example 52310 4-amino-5-(3-bromophenyl)-7-(2-N-pyrrolidinyl-5-thiazoyl)pyrido[2,3-d]pyrimidine

Procedure as found in Example 357 substituting pyrrolidine (Aldrich) for (2-methoxyethyl)methylamine in Example 521a. MS (DCI/NH₃) m/z 453/455 (M+H)⁺; IR (microscope) 3483, 3044, 1647, 1511, 1203 cm⁻¹.

15 Example 524

4-amino-5-(3-bromophenyl)-7-(2-N-methyl-N-propylamino-5-thiazoyl)pyrido[2,3-d]pyrimidine

Procedure as found in Example 357 substituting methylpropyl amine (Aldrich) for (2-methoxyethyl)methylamine in Example 521a to provide the title compound.

20 MS (DCI/NH₃) m/z 455/457 (M+H)⁺; IR (microscope) 3489, 3042, 1646, 1518, 1139 cm⁻¹.

Example 5254-amino-5-(3-bromophenyl)-7-(2-N,N-diethylamino-5-thiazoyl)pyrido[2,3-d]pyrimidine

Procedure as in Example 357 substituting diethylamine (Aldrich) for morpholine in Example 357a to provide the title compound. MS (DCI/NH₃) m/z 455/457 (M+H)⁺; IR (microscope) 3478, 3051, 1582, 1518, 1177 cm⁻¹.

Example 5264-amino-5-(3-bromophenyl)-7-(2-(N-methylpiperazinyl)-5-thiazoyl)pyrido[2,3-d]pyrimidine

30

Procedure as in Example 515 substituting the product from Example 526a for the product of Example 357b in Example 357c provided the title compound. MS (DCI/NH₃) m/z 482/484 (M+H)⁺; IR (microscope) 3469, 3053, 1645, 1500, 1002 cm⁻¹.

5 526a: 5-Acetyl-2-(4-methylpiperazine)thiazole

A solution of silicon tetraisothiocyanate (2.02 g, 7.76 mmol; Can. J. Chem. 1963, 41, 2123) in toluene (30 mL) was treated with a solution of N-methylpiperazine (3.50 mL, 31.6 mmol; Acros) in toluene (10 mL) and the mixture heated to 80 °C for 20 minutes.

The resulting mixture was concentrated, taken up in 10% water in isopropanol, refluxed

10 for 20 minutes, cooled and filtered. The filtrate was concentrated and recrystallized from isopropanol to provide 3.89 g (77%) of the desired compound. A solution of the 4-methylpiperazine-1-carbothioic acid amide (3.53 g, 22.2 mmol) and 2-bromo-3-oxobutyrinaldehyde (3.69 g, 22.2 mmol; Bull. Chem. Soc. Jpn. 1965, 38, 1158) in acetone was refluxed for 30 minutes. The reaction mixture was cooled, quenched with saturated 15 aqueous sodium carbonate and extracted with dichloromethane. The organic layers were combined, dried (Na₂SO₄), concentrated and the residue purified by silica gel chromatography (gradient elution with 30% acetone/dichloromethane to 5% methanol/dichloromethane) to provide 1.76 g (35%) of the desired compound as a yellow-brown solid.

20

Example 527

4-amino-5-(3-bromophenyl)-7-(2-(N-(2-pyridyl)piperazinyl)-5-thiazoyl)pyrido[2,3-d]pyrimidine

Procedure as in Example 515 substituting 1-(2-pyridyl)piperazine (Acros) for N-methylpiperazine in Example 526a. MS (ESI) m/z 545/547 (M+H)⁺; IR (microscope) 3484, 3049, 1651, 1495, 1053 cm⁻¹.

30

Example 528

4-amino-5-(3-bromophenyl)-7-(2-N-methy-N-(2-pyridylethyl)-5-thiazoyl)pyrido[2,3-d]pyrimidine

Procedure as in Example 515 substituting 2-(2-(methylamino)ethyl)pyridine dihydrochloride (Acros) for N-methylpiperazine in Example 526a. MS (DCI/NH₃) m/z 518/520 (M+H)⁺; IR (microscope) 3472, 3054, 1648, 1517, 1051 cm⁻¹.

5

Example 5294-amino-5-(3-bromophenyl)-7-(2-(4-oxopiperazinyl)-5-thiazoyl)pyrido[2,3-d]pyrimidine

A solution of the product from Example 506 (900 mg, 1.71 mmol) and tetrahydrofuran (12 mL) at room temperature was treated with 3 N hydrochloric acid (12 mL) and stirring continued for 24 hours. The reaction was made basic with sodium bicarbonate, extracted with dichloromethane, concentrated and the residue purified by 10 silica gel chromatography (elution with 5% methanol/dichloromethane) to provide 263 mg (32%) of the title compound. MS (DCI/NH₃) m/z 481/483 (M+H)⁺; IR (microscope) 3482, 3084, 1716, 1508, 1074 cm⁻¹.

15

Example 5304-amino-5-(3-bromophenyl)-7-(2-(4-(N-morpholinyl)iminopiperazinyl)-5-thiazoyl)pyrido[2,3-d]pyrimidine

A solution of Example 529 (200 mg, 0.415 mmol) and 4-aminomorpholine (Aldrich) in ethanol (5 mL) was heated to reflux for 5 hours. The solid was filtered and 20 dried to provide 140 mg (60%) of the title compound. MS (DCI/NH₃) m/z 565/567 (M+H)⁺; IR (microscope) 3485, 3051, 1644, 1506, 1111 cm⁻¹.

Example 5314-amino-5-(3-bromophenyl)-7-(6-N-morpholine-3-pyridinesulfonamide)pyrido[2,3-d]pyrimidine

Procedure as found in Example 357 substituting the product from Example 531b for the product from Example 357b in Example 357c. MS (DCI/NH₃) m/z 527/529 (M+H)⁺; IR (microscope) 3439, 3058, 1639, 1609, 1072 cm⁻¹.

30 531a: 5-Acetyl-2-thiopyridine

Δ solution of 5-acetyl-2-chloropyridine (10.11 g, 64.98 mmol; Tetrahedron 1992, 48, 9233) in ethanol was treated with thiourea (5.97 g, 78.4 mmol) and heated to reflux overnight. The reaction was cooled, the solid collected and taken up in 2 M sodium hydroxide. After stirring for 2 hours, the red solid was collected, acidified with glacial acetic acid. The yellow solid was collected and recrystallized from ethanol to provide 3.39 g (34%) of the desired compound.

MS (DCI/NH₃) m/z 154 (M+H)⁺.

531b: 5-Acetyl-2-morpholinopyridylsulfonamide

10 Δ suspension of the product from Example 531a (7.01 g, 45.7 mmol) in 1 M hydrochloric acid (60 mL) was treated with chlorine gas at 0 °C for 1 hour. The resulting solid was filtered, and taken up in dichloromethane (50 mL) and treated with morpholine (15 mL). After 1 hour, the mixture was quenched with 1 N hydrochloric acid and extracted with dichloromethane. The organic phases were combined, dried (Na₂SO₄) and concentrated. The residue was recrystallized from ethyl acetate to provide 6.31 g (59%) of the desired compound. MS (DCI/NH₃) m/z 271 (M+H)⁺.

Example 532

4-amino-5-(3-bromophenyl)-7-(2-(4-oxopiperidinyl)-5-pyrimidyl)pyrido[2,3-d]pyrimidine

20 Procedure as found in Example 529 substituting the product from Example 533c for the product from Example 506. MS (DCI/NH₃) m/z 476/478 (M+H)⁺; IR (microscope) 3469, 3051, 1644, 1561, 1108 cm⁻¹.

Example 533

25 4-amino-5-(3-bromophenyl)-7-(2-(4,4-dioxethylenepiperidinyl)-5-pyrimidyl)pyrido[2,3-d]pyrimidine

Procedure as found in Example 515 substituting the product from Example 533b for the product from Example 357b in Example 357c and formation of the salt by treatment with HCl in diethyl ether to provide the title compound. MS (DCI/NH₃) m/z 520/522 (M+H)⁺; IR (microscope) 3434, 3064, 1645, 1602, 1105 cm⁻¹.

533a: 5-bromo-2-(1,4-dioxa-8-azaspiro[4.5]decane)pyrimidine

5 A solution of 5-bromo-2-chloropyrimidine (3.09 g, 16.0 mmol; J. Chem. Soc. Chem. Commun. 1996, 2719) in ethanol (20 mL) at room temperature was treated with 1,4-dioxa-8-azaspiro[4.5]decane (6.00 mL, 46.8 mmol; Aldrich) and stirring continued overnight. The reaction mixture was neutralized with saturated aqueous sodium bicarbonate and extracted with dichloromethane. The organic phases were combined, dried (Na_2SO_4), concentrated and the residue purified by silica gel column chromatography (elution with 25% ethyl acetate/hexanes) to provide 4.78 g (99%) of the desired compound as a white solid. MS (DCI/NH₃) m/z 300/302 (M+H)⁺.

533b: 5-Acetyl-2-(1,4-dioxa-8-azaspiro[4.5]decane)pyrimidine

Procedure as found in Example 521b substituting the product from Example 533a for Example 521a to provide the desired compound. MS (DCI/NH₃) m/z 264 (M+H)⁺.

15

Example 534**4-amino-5-(3-bromophenyl)-7-(5-(1,4-dioxa-8-azaspiro[4.5]decan-8-yl)-2-pyrazinyl)pyrido[2,3-d]pyrimidine**

20 Procedure as found in Example 515 substituting the product from Example 534b for the product from Example 357b in Example 357c and formation of the salt by treatment with HCl in diethyl ether to provide the title compound. MS (DCI/NH₃) m/z 520/522 (M+H)⁺; IR (microscope) 3292, 3060, 1634, 1526, 1105 cm⁻¹.

534a: 5-Acetyl-2-chloropyrazine

25 A solution of 5-hydroxypyrazine-2-carboxylic acid (5.29 g, 37.76 mmol) in toluene was treated with thionyl chloride (9.00 mL, 123 mmol) and the mixture heated to reflux for 16 hours. The reaction mixture was concentrated and the residue taken up in dichloromethane (200 mL) and treated with a solution of N,O-dimethylhydroxylamine hydrochloride in 2 N sodium hydroxide. After 30 minutes, the layers were separated, the organic phase dried (Na_2SO_4) and concentrated. A portion of the amide (807 mg, 4.00

mmol) was taken up in tetrahydrofuran (20 mL) cooled to -10 °C and treated with methylmagnesium bromide (3 M in diethyl ether, 4.00 mL) and warmed to room temperature. The mixture was quenched with saturated aqueous ammonium chloride and extracted with ethyl acetate. The organic layers were dried (Na_2SO_4) and concentrated to provide 610 mg (97%) of the desired compound. ^1H NMR (CDCl_3 , 500 MHz) δ 9.00 (d, J = 1.1 Hz, 1 H), 8.63 (d, J = 1.1 Hz, 1 H), 2.70 (s, 3 H).

534b: 5-Acetyl-2-(1,4-dioxa-8-azaspiro[4.5]decane)pyrazine

Procedure as found in Example 511a substituting the product from Example 534a for 5-acetyl-2-bromothiophene and 1,4-dioxa-8-azaspiro[4.5]decane for morpholine. MS (DCI/NH₃) m/z 264 ($\text{M}+\text{H}$)⁺.

Example 535

4-amino-5-(3-bromophenyl)-7-(5-(4-oxopiperidinyl)-2-pyrazinyl)pyrido[2,3-d]pyrimidine

15 Procedure as found in Example 529 substituting the product from Example 534c for the product from Example 506 to provide the title compound. MS (DCI/NH₃) m/z 476/478 ($\text{M}+\text{H}$)⁺; IR (microscope) 3470, 3085, 1721, 1542, 1184 cm^{-1} .

Example 536

20 4-amino-5-(3-bromophenyl)-7-(6-N-cyclopropyl-3-pyridinesulfonamide)pyrido[2,3-d]pyrimidine

Procedure as found in Example 534c substituting cyclopropyl amine (Aldrich) for morpholine in Example 534b. MS (DCI/NH₃) m/z 497/357 ($\text{M}+\text{H}$)⁺; IR (microscope) 3441, 3059, 1640, 1609, 1177 cm^{-1} .

25

Example 537

4-amino-5-(3-bromophenyl)-7-(6-(N-1,4-dioxa-8-azaspiro[4.5]decane-8-yl)-3-pyridylsulfonamide)pyrido[2,3-d]pyrimidine

Procedure as found in Example 534 substituting 1,4-dioxa-8-azaspiro[4.5]decane (Aldrich) for morpholine in Example 534b. MS (DCI/NH₃) m/z 583/585 (M+H)⁺; IR (microscope) 3483, 3060, 1567, 1355, 1101 cm⁻¹.

5

Example 5384-amino-5-(3-bromophenyl)-7-(2-(4-(4-tetrahydropyranloxy)iminopiperidinyl)-5-pyrazinyl)pyrido[2,3-d]pyrimidine

Procedure as found in Example 530 substituting the product from 532 for the product from Example 529 and 0-(tertahydro-2H-pyran-4-yl)hydroxylamine

10 hydrochloride (JP07173169; CAN 123:313629) for 4-aminomorpholine. MS (DCI/NH₃) m/z 575/577 (M+H)⁺; IR (microscope) 3486, 3055, 1601, 1515, 1345 cm⁻¹.

Example 5394-amino-5-(3-bromophenyl)-7-(6-(4-(phenylmethoxy)iminopiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine

Prepared as described for Example 359, substituting O-Benzylhydroxylamine hydrochloride for ethoxyamine hydrochloride.

MS (DCI/NH₃) m/z 580/582 (M+H; ⁷⁹Br/⁸¹Br); IR (microscope) 3486, 3297, 3060, 1603, 1579, 1557 cm⁻¹.

20

Example 5404-amino-5-(3-bromophenyl)-7-(6-(4-(tert-butyloxy)iminopiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine

Prepared as described for Example 359, substituting O-(tert-butyl)hydroxylamine hydrochloride for ethoxyamine hydrochloride.

MS (DCI/NH₃) m/z 546/548 (M+H; ⁷⁹Br/⁸¹Br); IR (microscope) 3488, 3301, 3037, 1602, 1560, 1512 cm⁻¹.

Example 541

4-amino-5-(3-bromophenyl)-7-(6-(4-(cyclohexyloxy)iminopiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine

Prepared as described for Example 359, substituting O-Cyclohexylhydroxylamine hydrochloride, synthesized by the procedure of Grochowski, E; Jurczak. J. Synthesis 1976, 682 and starting with cyclohexanol, for ethoxyamine hydrochloride. MS (DCI/NH₃) m/z 572/574 (M+H; ⁷⁹Br/⁸¹Br); IR (microscope) 3485, 3297, 2931, 1555, 1517, 1349 cm⁻¹.

Example 542

10 4-amino-5-(3-bromophenyl)-7-(6-(4-hydroxyiminopiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine

Prepared as described for Example 359, substituting Hydroxylamine hydrochloride for ethoxyamine hydrochloride. MS (DCI/NH₃) m/z 490/492 (M+H; ⁷⁹Br/⁸¹Br); IR (microscope) 3444, 3020, 2819, 1646, 1505, 1546 cm⁻¹.

Example 543

20 4-amino-5-(3-bromophenyl)-7-(6-(4-(4-tetrahydropyran-4-yloxy)iminopiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine

Prepared as described for Example 359, substituting 4-tetrahydropyran-4-yloxyamine hydrochloride, synthesized by the procedure of Grochowski, E; Jurczak. J. Synthesis 1976, 682 and starting with Tetrahydro-4H-pyran-4-ol, for ethoxyamine hydrochloride. MS (DCI/NH₃) m/z 574/576 (M+H; ⁷⁹Br/⁸¹Br); IR (microscope) 3484, 3297, 3157, 2954, 1582, 1555 cm⁻¹.

25

Example 544

4-amino-5-(3-bromophenyl)-7-(6-(4-methoxyethoxyiminopiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine

Prepared as described for Example 359, substituting O-(2-methoxyethyl)hydroxylamine hydrochloride, synthesized by the procedure of Grochowski.

E; Jurczak, J. Synthesis 1976, 682 and starting with 2-Methoxyethanol, for ethoxyamine hydrochloride.

MS (DCI/NH₃) m/z 548/550 (M+H; ⁷⁹Br/⁸¹Br); IR (microscope) 3485, 3298, 3042, 1582, 1555, 1517 cm⁻¹.

5

Example 545

4-amino-5-(3-bromophenyl)-7-(6-(4-(2-thenylmethoxy)iminopiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine

Prepared as described for Example 359, substituting O-(2-thienylmethyl)hydroxylamine hydrochloride, synthesized by the procedure of Grochowski, E; Jurczak, J. Synthesis 1976, 682 and starting with 2-Thiophenemethanol, for ethoxyamine hydrochloride.

MS (DCI/NH₃) m/z 586/588 (M+H; ⁷⁹Br/⁸¹Br); IR (microscope) 3485, 3298, 3068, 1579, 1556, 1507 cm⁻¹.

15

Example 546

4-amino-5-(3-bromophenyl)-7-(6-(4-(4'-(5'H-2-oxyfuranyl)-4-hydroxypiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine

Prepared as described for Example 370 except substituting 4-(4'-(5'H-2-oxyfuranyl)-4-hydroxypiperidine for 4-methoxypiperidine, which was made as follows: to a solution of 4-bromo-2-triisopropylsiloxyfuran (5.0 g, 15.7 mmol; made according to G. Jas, Synthesis 1991, 965) in THF (50 mL) at -78 °C, a solution of t-butyllithium (1.7 M, 15 mL, 25.5 mmol) was added dropwise for 40 min. A solution of N-benzylpiperidin-4-one (4.4 mL, 23.8 mmol) was added at -78 °C. The reaction mixture was then allowed to warm up over night. Standard work-up. Column chromatographic separation (SiO₂, ethyl acetate : hexane = 1 : 2) gave 4.72 g product (70%). The product was then deprotected under H₂ in the presence of Pd(OH)₂, Et₃N in methanol.

MS (ESI): 559/561 (M+H; ⁷⁹Br/⁸¹Br).

IR (Mic): Vmax: 3432, 3309, 3204, 2928, 1744, 1634, 1605, 1372 cm⁻¹

30

Example 547 4-amino-5-(3-bromophenyl)-7-(6-(4-(1-(4-tetrahydropyranoyloxy)iminoethyl)-4-hydroxypiperidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine

Prepared as described for Example 559 except substituting Example 548 for
5 Example 562.

MS (ESI): 619/621 (M+H; $^{79}\text{Br}^{81}\text{Br}$).

IR (Mic): Vmax: 3485, 3310, 3204, 2955, 2849, 1682, 1615, 1578, 1552, 1461, 1353, 1135, 1066 cm^{-1} .

10 Example 548

4-amino-5-(3-bromophenyl)-7-(6-(4-(4'-acetyl-4'-hydroxypiperidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine

Prepared as described for Example 367 except substituting 4-acetyl-4-hydroxypiperidine for (1S,4S)-2-aza-5-oxa-bicyclo[2.2.1]heptane, which was prepared as
15 described in Example 562.

MS (ESI): 520/522 (M+H; $^{79}\text{Br}^{81}\text{Br}$).

IR (Mic): Vmax: 3472, 3385, 3298, 3090, 2953, 1711, 1644, 1578, 1562, 1483, 1464, 1353 cm^{-1} .

20 Example 549 4-amino-5-(3-bromophenyl)-7-(6-(4-(1-(isopropylcarboxymethoxy)iminoethyl)-4-hydroxypiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine

Prepared from Example 562 as described in Example 559; substituting
carboxymethoxylamine (Aldrich) for 4-tetrahydropyranoxyamine hydrochloride in
25 isopropanol as solvent

MS (ESI): 634/636 (M+H; $^{79}\text{Br}^{81}\text{Br}$).

IR (Mic): Vmax: 3450, 3311, 3174, 3068, 2984, 2937, 1737, 1674, 1647, 1606, 1555, 1440, 1373, 1201, 1136 cm^{-1} .

Example 5504-amino-5-(3-bromophenyl)-7-(6-(4-(1-(ethylcaboxymethoxy)iminoethyl))-4-hydroxypiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine

Prepared from Example 562 as described in Example 559; substituting
5 carboxymethoxylamine (Aldrich) for 4-tetrahydropyranoxyamine hydrochloride in ethanol
as solvent.

MS (ESI): 620/622 (M+H; $^{79}\text{Br}^{81}\text{Br}$).

IR (Mic): Vmax: 3449, 3313, 3178, 3066, 2985, 1745, 1674, 1648, 1607, 1444, 1371,
1200, 1135 cm^{-1} .

10

Example 5514-amino-5-(3-bromophenyl)-7-(6-(4-(1-(methylcaboxymethoxy)iminoethyl))-4-hydroxypiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine

Prepared from Example 562 as described in Example 559; substituting
15 carboxymethoxylamine (Aldrich) for 4-tetrahydropyranoxyamine hydrochloride in
methanol as solvent.

MS (ESI): 606/608 (M+H; $^{79}\text{Br}^{81}\text{Br}$).

IR (Mic): Vmax: 3450, 3309, 3067, 2957, 2933, 1751, 1675, 1647, 1605, 1439, 1368,
1200, 1134 cm^{-1} .

20

Example 5524-amino-5-(3-bromophenyl)-7-(6-(4-(1-(2-tetrahydropyranloxy)iminoethyl))-4-hydroxypiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine

Prepared from Example 562 as described in Example 559; substituting O-
25 (tetrahydro-2H-pyran-2-yl)hydroxylamine (Aldrich) for 4-tetrahydropyranoxyamine
hydrochloride.

MS (ESI): 618/620 (M+H; $^{79}\text{Br}^{81}\text{Br}$).

IR (Mic): Vmax: 3449, 3306, 3197, 3066, 2949, 2872, 1675, 1648, 1607, 1442, 1370,
1200, 1135 cm^{-1} .

30

Example 553 4-amino-5-(3-bromophenyl)-7-(6-(4-(1-(allyloxy)iminoethyl))-4-hydroxypiperidinyl)-3-pyridylpyrido[2,3-d]pyrimidine

Prepared from Example 562 as described in Example 559; substituting 2-propen-1-oxylamine (Aldrich) for 4-tetrahydropyranoxyamine hydrochloride.

5 MS (ESI): 574/576 (M+H; $^{79}\text{Br}^{81}\text{Br}$).

IR (Mic): Vmax: 3450, 3309, 3175, 3071, 2930, 2871, 1673, 1647, 1605, 1515, 1435, 1200, 1134 cm^{-1} .

Example 554 4-amino-5-(3-bromophenyl)-7-(6-(4-(1-(ethoxy)iminoethyl))-4-hydroxypiperidinyl)-3-pyridylpyrido[2,3-d]pyrimidine

10 Prepared from Example 562 as described in Example 559; substituting ethoxylamine (Aldrich) for 4-tetrahydropyranoxyamine hydrochloride

MS (ESI): 562/564 (M+H; $^{79}\text{Br}^{81}\text{Br}$).

IR (Mic): Vmax: 3451, 3311, 3063, 2979, 2936, 2881, 1673, 1647, 1606, 1368, 1200,

15 1183, 1133 cm^{-1} .

Example 555 0.6)

4-amino-5-(3-bromophenyl)-7-(6-(4-(1-(methoxy)iminoethyl))-4-hydroxypiperidinyl)-3-pyridylpyrido[2,3-d]pyrimidine

20 Prepared from Example 562 as described in Example 559; substituting methoxylamine (Aldrich) for 4-tetrahydropyranoxyamine hydrochloride.

MS (ESI): 548/550 (M+H; $^{79}\text{Br}^{81}\text{Br}$).

IR (Mic): Vmax: 3450, 3312, 3064, 2965, 2820, 1674, 1646, 1444, 1369, 1199, 1135, 1045 cm^{-1} .

25

Example 556 4-amino-5-(3-bromophenyl)-7-(6-(4-(1-(hydroxy)iminoethyl))-4-hydroxypiperidinyl)-3-pyridylpyrido[2,3-d]pyrimidine

Prepared from Example 562 as described in Example 559; substituting hydroxylamine (Aldrich) for 4-tetrahydropyranoxyamine hydrochloride.

30

MS (ESI): 534/536 (M+H: $^{79}\text{Br}^{81}\text{Br}$).

IR (Mic): Vmax: 3448, 33133198, 3070, 2881, 1782, 1676, 1650, 1610, 1448, 1371, 1200, 1137 cm^{-1} .

5

Example 557

4-amino-5-(3-bromophenyl)-7-(6-(4-(2-tetrahydropyranloxy)iminopiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine

Prepared from Example 328 as described in Example 559; substituting O-(tetrahydro-2H-pyran-2-yl)hydroxylamine (Aldrich) for 4-tetrahydropyranoxyamine hydrochloride.

MS (ESI): 574/576 (M+H: $^{79}\text{Br}^{81}\text{Br}$).

IR (Mic): Vmax: 3437, 3304, 3057, 2955, 2859, 2684, 1639, 1605, 1441, 1368, 1238, 1068 cm^{-1} .

15

Example 558

4-amino-5-(3-bromophenyl)-7-(6-(4-(isopropylcarboxymethoxy)iminopiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine

Prepared from Example 328 as described in Example 559; substituting Example 328 for Example 562 and substituting carboxymethoxylamine (Aldrich) for 4-tetrahydropyranoxyamine hydrochloride in isopropanol as solvent.

MS (ESI): 590/592 (M+H: $^{79}\text{Br}^{81}\text{Br}$).

IR (Mic): Vmax: 3487, 3389, 3301, 3152, 3058, 2979, 2928, 2873, 1749, 1603, 1580, 1557, 1508, 1414, 1348, 1233, 1101 cm^{-1} .

25

Example 559

4-amino-5-(3-bromophenyl)-7-(6-(4-hydroxy-4-(1-(4-tetrahydropyranloxy)iminoethyl))-4-hydroxypiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine

Prepared from Example 562 as follows: to a solution of Example 562 (250 mg, 0.48 mmol) in ethanol (10 mL), 4-tetrahydropyranoxyamine hydrochloride (80 mg, 0.5 mmol; made as described from: JP 94-177353 19940729 and prepared in Example 543)

was added, followed by concentrated HCl (2 drops). The mixture was heated to reflux for about 10 hours. Standard work up, followed by chromatography (SiO₂, 5% MeOH in CH₂Cl₂) gave 156 mg (53%) of the title compound.

MS (ESI): 618/620 (M+H; ⁷⁹Br/⁸¹Br).

5 IR (Mic): Vmax: 3488, 3304, 3199, 2954, 2855, 1603, 1578, 1557, 1509, 1352, 1233, 1066 cm⁻¹.

Example 560

4-amino-5-(3-bromophenyl)-7-(6-(4-(3-butyrolactone)-4-hydroxypiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine

10

Prepared as described for Example 370 except substituting 4-(4-hydroxypiperidin-4-yl)butyrolactone for 4-methoxypiperidine, which was made as follows: to a solution of 3-ethoxycarboxylpropyl triphenylphosphonium bromide (10.0 g, 22 mmol) in THF, a solution of potassium bis(trimethylsilyl)amide (0.5 M, 52 mL, 26 mmol) was added at - 78 °C. the reaction mixture was allowed to stir for 40 min at - 78 °C. N-benzyl-4-piperidinone (4.5 mL, 24 mmol) was added. The mixture stirred at -78 °C for 3 hours and then gradually warmed up to room temperature over night. Standard work up followed by chromatography (SiO₂, ethyl acetate: hexanes = 1:4) to give 5.01g product (83%). The product was then dihydroxylated as described in Example 565, and treated with p-toluenesulfonic acid in benzene to give the lactone. Debenzylation via hydrogenation gave the desired amine.

MS (ESI): 561/563 (M+H; ⁷⁹Br/⁸¹Br).

IR (Mic): Vmax: 3479, 3311, 3056, 2942, 2853, 2726, 1777, 1654, 1574, 1556, 1503, 1408, 1354 cm⁻¹.

25

Example 561

4-amino-5-(3-bromophenyl)-7-(6-(4-(2-butyrolactone)-4-hydroxypiperidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine

Prepared as described for Example 367 except substituting 2-(4-hydroxypiperidin-4-yl)butyrolactone for (1S,4S)-2-aza-5-oxa-bicyclo[2.2.1]heptane,

which was made from a-(1-benzyl-4-hydroxy-4-piperidyl)-*g*-butarolactone (Salor) via hydrogenation.

MS (ESI): 562/564 (M+H; $^{79}\text{Br}/^{81}\text{Br}$).

IR (Mic): Vmax: 3484, 3289, 3054, 2928, 1768, 1644, 1575, 1464, 1358, 1264, 1138 cm^{-1} .

5

Example 562

4-amino-5-(3-bromophenyl)-7-(6-(4-acetyl-4-hydroxypiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine

Prepared as described for Example 370 except substituting 4-acetyl-4-hydroxypiperidine for 4-methoxypiperidine, which was prepared as follows: to a solution of ethyl vinyl ether (3.8 mL, 40 mmol) in THF, a solution of t-butylolithium (1.7 M, 24 mL, 40 mmol) was added at -78 °C. The reaction mixture was warmed up to 0 °C for about 30 min, and cooled down to -78 °C again before transferred to a slurry of CeCl_3 (10 g, 40 mmol) in THF at -78 °C. The mixture was stirred at -78 °C for about 1 hour, and a cold solution of N-benzyl-4-piperidinone (5.5 mL, 30 mmol) in THF was added. The reaction mixture was then gradually warmed up over night. Standard work up, followed by chromatography (SiO_2 , 1% MeOH in CH_2Cl_2) to give 7.1 g product (91%). The product was then hydrolysed to ketone product in the presence of MeOH/THF/ CH_2Cl_2 (20:30:5) mixture solvents and HCl (3N, 7 mL) at 0 °C. The product was then deprotected via hydrogenation to give the final keto-amine.

MS (ESI): 519/521 (M+H; $^{79}\text{Br}/^{81}\text{Br}$).

IR (Mic): Vmax: 3486, 3312, 3210, 2950, 2923, 2859, 1706, 1604, 1580, 1558, 1508, 1352, 1242 cm^{-1} .

25

Example 563

4-amino-5-(3-bromophenyl)-7-(6-(3-hydroxyazetidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine

Prepared as described for Example 370 except substituting 3-hydroxyazetidine for 4-methoxypiperidine, which was prepared from the N-diphenylmethyl-4-hydroxyaziridine (Maybridge) via hydrogenation.

MS (ESI): 449/451 (M+H; $^{79}\text{Br}^{81}\text{Br}$).

IR (Mic): Vmax: 3471, 3301, 3061, 1602, 1580, 1558, 1354 cm^{-1} .

Example 564

5 4-amino-5-(3-bromophenyl)-7-(6-((1R,5S)-3-hydroxy-8-azabicyclo[3.2.1]octan-8-yl)-3-pyridyl)pyrido[2,3-d]pyrimidine

Prepared as described for Example 370 except (1R,5S)-8-azabicyclo[3.2.1]octan-3-ol for 4-methoxypiperidine, which was prepared from tropanone as described by A.H. Newman, et al, J. Med. Chem. 1995, 38, 3933.

10 MS (ESI): 503/505 (M+H; $^{79}\text{Br}^{81}\text{Br}$).

IR (Mic): Vmax: 3480, 3317, 3204, 2918, 1706, 1603, 1580, 1558, 1352, 1243 cm^{-1} .

Example 565

15 4-amino-5-(3-bromophenyl)-7-(6-(cis-2,3-dihydroxypiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine

Prepared from Example 567 as follows: to a solution of Example 567 (600 mg, 1.31 mmol) in THF/MeOH (55:5), NMO (460 mg, 3.93 mmol) was added followed by OsO₄ (35 mg, 0.14 mmol). The reaction mixture was allowed to stir over night. Quenched with sodium thiosulfate. Standard work up, followed by chromatography (SiO₂, 10% MeOH in

20 CH_2Cl_2) to give 260 mg (40%) of the title compound.

MS (ESI): 493/495 (M+H; $^{79}\text{Br}^{81}\text{Br}$).

IR (Mic): Vmax: 3478, 3296, 3082, 2924, 1641, 1604, 1581, 1554, 1513, 1354, 1227 cm^{-1} .

25 Example 566 4-amino-5-(3-bromophenyl)-7-(6-(N-methyl-N-(3-pyridyl)methyl)amino)-3-pyridazinyl)pyrido[2,3-d]pyrimidine

Prepared as described for Example 367 except substituting 3-(methylaminomethyl)pyridine (Maybridge) for (1S,4S)-2-aza-5-oxa-bicyclo[2.2.1]heptane.

30 MS (ESI): 499/501 (M+H; $^{79}\text{Br}^{81}\text{Br}$).

IR (Mic): Vmax: 3475, 3300, 3151, 3061, 2928, 1682, 1555, 1484, 1395, 1352 cm⁻¹.

Example 567

4-amino-5-(3-bromophenyl)-7-(6-(1,2,3,6-tetrahydropyridyl)-3-pyridyl)pyrido[2,3-d]pyrimidine

5

Prepared as described for Example 370 except substituting 1,2,3,6-tetrahydropyridine (Aldrich) for 4-methoxy piperidine.

MS (ESI): 459/461 (M+H; ⁷⁹Br/⁸¹Br).

IR (Mic): Vmax: 3473, 3305, 3090, 2928, 1670, 1578, 1558, 1508, 1355, 1244 cm⁻¹.

10

Example 568

4-amino-5-(3-bromophenyl)-7-(6-(4-(N-4'methoxyphenylcarbamoyl)piperidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine

15 Prepared as described for Example 367 except substituting 4-(N-4'methoxyphenylcarbamoyl)piperidine for (1S,4S)-2-aza-5-oxa-bicyclo[2.2.1]heptane, which was prepared prepared as described in Example 570 from N-benzyl-4-hydroxypiperidine.

MS (ESI): 459/461 (M+H; ⁷⁹Br/⁸¹Br).

IR (Mic): Vmax: 3473, 3305, 3090, 2928, 1649, 1581, 1560, 1508, 1355 cm⁻¹.

20

Example 569

4-amino-5-(3-bromophenyl)-7-(6-(4-(2-butyrolactone)-4-hydroxypiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine

25 Prepared as described for Example 370 except substituting 2-(4-hydroxypiperidinyl)butyrolactone for 4-methoxypiperidine, which was made from a-(1-benzy1-4-hydroxy-4-piperidyl)-g-butrolactone (Salor) via hydrogenation.

MS (ESI): 561/563 (M+H; ⁷⁹Br/⁸¹Br).

IR (Mic): Vmax: 3462, 3392, 3297, 3256, 3108, 2948, 2859, 1765, 1638, 1598, 1579, 1556, 1505, 1355, 1240, 1158 cm⁻¹.

30

Example 5704-amino-5-(3-bromophenyl)-7-(6-(trans-3,4- bis(N-4'-methoxyphenylcarbamoyl)pyrrolidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine

Prepared as described for Example 370 except substituting 3R,4R-bis(N-4'-methoxyphenylcarbamoyl)pyrrolidine for 4-methoxypiperidine, which was made as follows: N-benzyl-3R,4R-dihydroxypyrrrolidine (500 mg, 2.6 mmol) (Digital) was dissolved in CH_2Cl_2 (50 mL), 4-methoxyphenylisocyanate was added at room temperature. The reaction mixture was then allowed to stir for about 8 hours. White precipitate was collected, and washed with hexanes to give a pure product (1.23 g, 96%). The benzyl group was then deprotected via hydrogenation.

10 MS (ESI): 777/779 ($\text{M}+\text{H}$; $^{79}\text{Br}^{61}\text{Br}$).
IR (Mic): Vmax: 3481, 3302, 3194, 3057, 2955, 2838, 1726, 1604, 1555, 1514, 1415, 1228, 1076, 1030, 829 cm^{-1} .

15 Example 571

4-amino-5-(3-bromophenyl)-7-(6-((1S,5R)-3-hydroxy-8-azabicyclo[3.2.1]octan-8-yl)-3-pyridyl)pyrido[2,3-d]pyrimidine

Prepared as described for Example 370 except substituting (1S,5R)-8-azabicyclo[3.2.1]octan-3-ol for 4-methoxypiperidine, which was made from tropane 20 (Aldrich) as described by A.H. Newman, et al. (J. Med. Chem. 1995, 38, 3933).
MS (ESI): 503/505 ($\text{M}+\text{H}$; $^{79}\text{Br}^{61}\text{Br}$).
IR (Mic): Vmax: 3472, 3303, 3157, 2939, 1681, 1600, 1580, 1554, 1354 cm^{-1} .

Example 572

25 4-amino-5-(3-bromophenyl)-7-(6-(S,S-trans-3,4-dihydroxypyrrrolidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine

Prepared as described for Example 370 except substituting 3S,4S-dihydroxypyrrrolidine for 4-methoxypiperidine which was prepared from the benzylprotected form (Digital) as described in Example 574.

30 30 MS (ESI): 479/481 ($\text{M}+\text{H}$; $^{79}\text{Br}^{61}\text{Br}$).

IR (Mic): Vmax: 3484, 3299, 3193, 2928, 2854, 1629, 1584, 1561, 1536, 1513, 1435, 1078 cm⁻¹.

Example 573

5 4-amino-5-(3-bromophenyl)-7-(6-(R,R-trans-3,4-dihydroxypyrrolidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine

Prepared as described for Example 367 except substituting 3R,4R-dihydroxypyrrolidine for "(1S,4S)-2-aza-5-oxa-bicyclo[2.2.1]heptane" which was made as described in Example 574

10 10 MS (ESI): 480/482 (M+H; ⁷⁹Br/⁸¹Br).

IR (Mic): Vmax: 3484, 3302, 3209, 3077, 2932, 2724, 1628, 1599, 1585, 1562, 1514, 1433 cm⁻¹.

Example 574

15 4-amino-5-(3-bromophenyl)-7-(6-(R,R-trans-3,4-dihydroxypyrrolidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine

Prepared as described for Example 370 except substituting 3R,4R-dihydroxypyrrolidine for 4-methoxypiperidine and was prepared as follows: To a solution of N- benzyl-3R,4R-dihydroxypyrrolidine (Digital; 1.4 g, 7.25 mmol) in methanol, 20 Pd(OH)₂ on carbon (300 mg) was added followed by H₂ (1 atom.) at room temperature over night. Standard work up gave 635 mg of the product (85%).

MS (ESI): 479/481 (M+H; ⁷⁹Br/⁸¹Br).

IR (Mic): Vmax: 3484, 3303, 3208, 2932, 2861, 1585, 1562, 1538, 1513, 1434, 1078 cm⁻¹.

25

Example 575

4-amino-5-(3-bromophenyl)-7-(6-(4-oxo-1-phenyl-1,3,8-triazaspiro[4.5]decan-8-yl)-3-pyridyl)pyrido[2,3-d]pyrimidine

Prepared as described for Example 370 except 1-phenyl-1,3,8-triazaspiro[4.5]decan-4-one (Acros) for 4-methoxypiperidine.

MS (ESI): 607/609 (M+H; $^{79}\text{Br}^{81}\text{Br}$).

IR (Mic): Vmax: 3427, 3321, 3055, 1776, 1644, 1607, 1533, 1445, 1373, 1246 cm^{-1} .

Example 576

5 4-amino-5-(3-bromophenyl)-7-(6-(1-oxa-4-oxo-4-thia-8-azaspiro[4.5]decan-8-yl)-3-pyridyl)pyrido[2,3-d]pyrimidine

Prepared from Example 586 as follows: to a solution of Example 586 (250 mg, 0.47 mmol) in CH_2Cl_2 at 0 °C, mCPBA was added in small portion. The reaction was monitored by TLC. After reaction completion, quenched with sodium thiosulfate.

10 Standard work-up, followed by chromatography purification (SiO_2 , 10% MeOH in CH_2Cl_2) to give 152 mg of the title compound (59%).

MS (ESI): 551/553 (M+H; $^{79}\text{Br}^{81}\text{Br}$).

IR (Mic): Vmax: 3474, 3384, 3305, 3062, 2918, 1603, 1581, 1561, 1511, 1413, 1352, 1228 cm^{-1} .

15

Example 577

4-amino-5-(3-bromophenyl)-7-(6-(1-oxa-4,4-dioxido-4-thia-8-azaspiro[4.5]decan-8-yl)-3-pyridyl)pyrido[2,3-d]pyrimidine

Prepared from Example 586 as follows: to a solution of Example 586 (300 mg, 0.56 mmol) in acetic acid at 0 °C, a solution of KMnO_4 in water was added till the color stayed. Quenched with sodium thiosulfate. Standard work up, followed by chromatography separation (SiO_2 , 5% MeOH in CH_2Cl_2) to give 151 mg of the title compound (48%).

MS (ESI): 567/569 (M+H; $^{79}\text{Br}^{81}\text{Br}$).

IR (Mic): Vmax: 3475, 3348, 3210, 3061, 2955, 1694, 1585, 1308, 1235 cm^{-1} .

25

Example 578

4-amino-5-(3-bromophenyl)-7-(6-(4-oxo-1-phenyl-1,3,8-triazaspiro[4.5]dec-2-en-8-yl)-3-pyridyl)pyrido[2,3-d]pyrimidine

Prepared as described for Example 370 except substituting 1-phenyl-1,3,8-30 triazaspiro[4.5]dec-2-en-4-one for 4-methoxypiperidine as follows: 1-phenyl-1,3,8-

triazaspiro[4,5]decaN-4-one (Acros, 350 mg, 1.5 mmol) was used to react with the chloride intermediate (200 mg, 0.48 mmol) in DMSO at 100 °C for over night. There were two major products, one of them was the desired compound (95 mg, 33%).

MS (ESI): 605/607 (M+H; $^{79}\text{Br}^{81}\text{Br}$).

5 IR (Mic): Vmax: 3486, 3325, 3194, 3056, 2957, 2870, 1719, 1602, 1580, 1559, 1533, 1353, 1256 cm^{-1} .

Example 579

4-amino-5-(3-bromophenyl)-7-(6-(4-(2-keto-1-benzimidazoliny)l)piperidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine

10 Prepared as described for Example 367 except substituting 4-(2-keto-1-benzimidazoliny)l)piperidine (Aldrich) for “(1S,4S)-2-aza-5-oxa-bicyclo[2.2.1]heptane”.

MS (ESI): 594/596 (M+H; $^{79}\text{Br}^{81}\text{Br}$).

IR (Mic): Vmax: 3435, 3347, 3063, 1690, 1631, 1610, 1554, 1484, 1375 cm^{-1} .

15

Example 580

4-amino-5-(3-bromophenyl)-7-(6-(4-oxothiomorpholiny)-3-pyridyl)pyrido[2,3-d]pyrimidine

20 Prepared from Ex. 328 as follows: to a solution of Example328 (400 mg, 0.84 mmol) in acetic acid, H_2O_2 (30%) was added till all the starting material was converted to the desired product. Standard work up, followed by chromatography (SiO_2 , 10% MeOH in CH_2Cl_2) gave 301 mg of the title compound (72%).

MS (ESI): 495/497 (M+H; $^{79}\text{Br}^{81}\text{Br}$).

IR (Mic): Vmax: 3440, 3060, 2869, 1695, 1645, 1606, 1484, 1372, 1243 cm^{-1} .

25 MS (ESI): 495/497 (M+H; $^{79}\text{Br}^{81}\text{Br}$).

Example 581

4-amino-5-(3-bromophenyl)-7-(6-(4-(2-keto-1-benzimidazoliny)l)piperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine

Prepared as described for Example 370 except substituting 4-(2-keto-1-benzimidazoliny) piperidine (Aldrich) for 4-methoxypiperidine.

MS (ESI): 593/595 (M+H; $^{79}\text{Br}^{81}\text{Br}$).

IR (Mic): Vmax: 3473, 3304, 3063, 2918, 1603, 1581, 1512, 1413, 1353, 1228 cm^{-1} .

5

Example 582

4-amino-5-(3-bromophenyl)-7-(6-(N-methyl-N-(2-pyridylethyl)amino)-3-pyridyl)pyrido[2,3-d]pyrimidine

Prepared as described for Example 370 except substituting 2-(2'-methylaminoethyl)pyridine (Aldrich) for 4-methoxypiperidine.

MS (ESI): 512/514 (M+H; $^{79}\text{Br}^{81}\text{Br}$).

IR (Mic): Vmax: 3475, 3303, 3046, 2931, 1648, 1583, 1561, 1519, 1405, 1354, 1142 cm^{-1} .

15

Example 583

4-amino-5-(3-bromophenyl)-7-(6-(N-methyl-N-(4-pyridylethyl)amino)-3-pyridyl)pyrido[2,3-d]pyrimidine

Prepared as described for Example 370 except substituting 4-(2'methylaminoethyl)pyridine (Aldrich) for 4-methoxypiperidine.

MS (ESI): 512/514 (M+H; $^{79}\text{Br}^{81}\text{Br}$).

IR (Mic): Vmax: 3480, 3252, 3000, 1600, 1590, 1570, 1350 cm^{-1} .

25

Example 584

4-amino-5-(3-bromophenyl)-7-(6-N-(3-pyridylmethyl)amino-3-pyridyl)pyrido[2,3-d]pyrimidine

Prepared as described for Example 370 except substituting 3-(aminomethyl)pyridine (Aldrich) for 4-methoxypiperidine.

MS (ESI): 484/486 (M+H; $^{79}\text{Br}^{81}\text{Br}$).

IR (Mic): Vmax: 3477, 3289, 3233, 3040, 1640, 1610, 1558, 1480, 1392, 1353, 1310, 1145 cm^{-1} .

Example 5854-amino-5-(3-bromophenyl)-7-(6-(2-hydroxymethylpiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine

5 Prepared as described for Example 370 except substituting 2-hydroxymethylpiperidine (Aldrich) for 4-methoxypiperidine.
MS (ESI): 491/493 (M+H; $^{79}\text{Br}^{81}\text{Br}$).
IR (Mic): Vmax: 3479, 3396, 3299, 3076, 2935, 2858, 1643, 1600, 1580, 1558, 1506, 1418, 1351 cm^{-1} .

10

Example 5864-amino-5-(3-bromophenyl)-7-(6-(1-oxa-4-thia-8-azaspiro[4.5]decan-8-yl)-3-pyridyl)pyrido[2,3-d]pyrimidine

15 Prepared from Ex. 328 as follows: to a slurry of Example 328 (1.0 g, 2.1 mmol) in CH_2Cl_2 (220 mL), thioethanol (295 mL, 4.2 mmol) was added followed by BF_3 etherate (535 mL, 4.2 mmol). The mixture stirred at room temperature for 1 day, and quenched with NaHCO_3 (sat.). Standard work up, the crude product mixture was then recrystallized from $\text{CH}_2\text{Cl}_2/\text{MeOH}/\text{hexanes}$ to give the title compound (902 mg, 80%).
MS (ESI): 535/537 (M+H; $^{79}\text{Br}^{81}\text{Br}$).
20 IR (Mic): Vmax: 3487, 3471, 3291, 3048, 2949, 2858, 1642, 1603, 1560, 1511, 1418, 1353, 1227, 1085 cm^{-1} .

Example 5874-amino-5-(3-bromophenyl)-7-(6-(4-hydroxy-4-(4-bromophenyl)piperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine

25 Prepared as described for Example 370 except substituting 4-(4'-bromophenyl)-4-hydroxypiperidine (Aldrich) for 4-methoxypiperidine.
MS (ESI): 633/635 (M+H; $^{79}\text{Br}^{81}\text{Br}$).
IR (Mic): Vmax: 3483, 3296, 3055, 2944, 1645, 1604, 1561, 1531, 1506, 1430, 1340, 30 1238 cm^{-1} .

Example 5884-amino-5-(3-bromophenyl)-7-(6-(4-N-(2-pyridinyl)piperazinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine

5 Prepared as described for Example 370 except substituting 1-(2'-pyridino)piperazine (Aldrich) for 4-methoxypiperidine.

MS (ESI): 539/541 (M+H; $^{79}\text{Br}^{81}\text{Br}$).

IR (Mic): Vmax: 3476, 3289, 3052, 2929, 2843, 1642, 1597, 1559, 1481, 1398, 1231 cm^{-1} .

10

Example 5894-amino-5-(3-bromophenyl)-7-(6-(4-N-(2-hydroxyethylthioethyl)piperazinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine

Prepared as described for Example 370 except substituting 1-(2-(2'-hydroxyethoxy)ethyl)piperazine (Aldrich) for 4-methoxypiperidine..

MS (ESI): 550/552 (M+H; $^{79}\text{Br}^{81}\text{Br}$).

IR (Mic): Vmax: 3490, 3396, 3279, 3143, 2919, 2852, 1633, 1604, 1582, 1555, 1504, 1424, 1337, 1241, 1119 cm^{-1} .

20

Example 5904-amino-5-(3-bromophenyl)-7-(6-(4,4-diacetoxyethylthio)piperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine

Prepared as described for Example 370 except substituting 4,4-di(2'-acetoxyetha-N-1-thio)piperidine for 4-methoxypiperidine. This amine was prepared was made as follows: 25 to a solution of 4-piperidinone hydrochloride salt (5.0 g, 32.6 mmol) in acetic acid (100 mL), 2-thioetha-N-1-ol (3 mL, 42.8 mmol) was added followed by BF_3 etherate (9.0 mL, 71.0 mmol) at room temperature. The reaction mixture was allowed to stir at room temperature for 3 days, and standard work-up gave a crude product 8.28 g (86%).
MS (ESI): 697/699 (M+H; $^{79}\text{Br}^{81}\text{Br}$).

IR (Mic): Vmax 3482, 3300, 3058, 2944, 2853, 1738, 1602, 1574, 1560, 1508, 1352, 1231 cm⁻¹.

Example 591

5 4-amino-5-(3-bromophenyl)-7-(6-(N-methy-N-(3-pyridylmethyl)amino)-3-pyridyl)pyrido[2,3-d]pyrimidine

Prepared as described for Example 370 except substituting 3-(methylaminomethyl)pyridine (Maybridge) for 4-methoxypiperidine. MS (ESI): 498/500 (M+H; ⁷⁹Br/⁸¹Br).

10 IR (Mic): Vmax: 3477, 3298, 3092, 2923, 1645, 1604, 1559, 1516, 1399, 1356 cm⁻¹.

Example 592

4-amino-5-(3-bromophenyl)-7-(6-(4-pyrrolidinylpiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine

15 Prepared as described for Example 370 except substituting 4-(1-pyrrolidinyl)piperidine (Aldrich) for 4-methoxypiperidine. MS (ESI): 554/556 (M+H; ⁷⁹Br/⁸¹Br).

IR (Mic): Vmax: 3474, 3299, 3042, 2807, 1647, 1601, 1574, 1560, 1507, 1231 cm⁻¹.

20 Example 593 4-amino-5-(3-bromophenyl)-7-(6-(2-(1H-imidazol-4-yl)ethylamino)-3-pyridazinyl)pyrido[2,3-d]pyrimidine

4-Amino-5-(3-bromophenyl)-7-(6-chloropyridaz-3-yl)pyrido[2,3-d]pyrimidine (165mg), prepared in Example 367, histamine (133mg), and potassium carbonate (166mg) were suspended in pyridine (2ml) and heated at 110°C for 20h. The reaction mixture was then directly chromatographed (TFA/MeOH/CH₂Cl₂) to give the title compound. mp: 83 235°C; MS (ESI)⁺ m/z: 488/490. IR (cm⁻¹): 3475, 3301, 3199, 1721, 1625, 1580, 1553, 1467, 1357, 1133.

Example 594

4-amino-5-(3-bromophenyl)-7-(6-(4-N-cyanomethylpiperazinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine

Prepared by deformylation of Example 329 with hydrochloric acid in methanol and followed by treatment with iodoacetyl nitrile in dimethylformamide.

5 IR (mic) 3473, 3299, 2822, 1561, 1234 cm^{-1} ;
MS m/z 502 (M+H)⁺.

Example 595

4-amino-5-(3-bromophenyl)-7-(6-(3-hydroxypyrroldinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine

10 Prepared as described for Example 370 except substituting 3-hydroxypyrroldine for 4-methoxypiperidine.

IR (microscope) 3480, 3300, 1606, 1559, 1431, 1309 cm^{-1} ;
MS m/z 463 (M+H)⁺.

15

Example 596

4-amino-5-(3-bromophenyl)-7-(6-(4-methylpiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine

20 Prepared as described for Example 370 except substituting 3-methylpiperidine for 4-methoxypiperidine.
IR (microscope) 3473, 3092, 1558, 1506, 1233 cm^{-1} ;
MS m/z 476 (M+H)⁺.

Example 597

25 4-amino-5-(3-bromophenyl)-7-(6-(cis-3,5-dimethylmorpholinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine

Prepared as described for Example 370 except substituting cis-3,5-dimethylmorpholine for 4-methoxypiperidine.

IR (microscope) 3475, 3090, 1561, 1508, 1239, 1175 cm^{-1}
30 MS m/z 492 (M+H)⁺.

Example 5984-amino-5-(3-bromophenyl)-7-(6-(4,4-difluoropipridinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine

5 Prepared as described for Example 370 except substituting 4,4-difluoropipridine for 4-methoxypiperidine, 4,4-difluoropipridine was prepared according to Tetrahedron, 1977, 33, 1707.

IR (microscope) 3474, 3091, 1507, 1237 cm^{-1} ; MS m/z 498 ($\text{M}+\text{H}$)⁺.

10

Example 5994-amino-5-(3-bromophenyl)-7-(6-(1,1-dioxidothiomorpholinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine

Prepared by the oxidation of Example 605 using OsO_4 in $\text{MeOH}/\text{CH}_2\text{Cl}_2/\text{acetone}$ (1:1:1) solution.

15 IR(KBr) 3470, 1600, 1564, 1316, 1287, 1122 cm^{-1} MS m/z 513 ($\text{M}+\text{H}$)⁺.Example 6004-amino-5-(3-bromophenyl)-7-(6-thiazolidinyl-3-pyridyl)pyrido[2,3-d]pyrimidine

20 Prepared according to the procedure of Example 306.

IR (microscope) 3468, 3052, 1557, 1509, 1407, 1289 cm^{-1} ; MS m/z 466 ($\text{M}+\text{H}$)⁺.Example 6014-amino-5-(3-bromophenyl)-7-(6-(1,1-dioxidothiazolidin-3-yl)-3-pyridyl)pyrido[2,3-d]pyrimidine

25 Prepared according to the procedure of Example 306.

IR (microscope) 3466, 3090, 1563, 1508, 1234 cm^{-1} ; MS m/z 498 ($\text{M}+\text{H}$)⁺.Example 60230 4-amino-5-(3-bromophenyl)-7-(6-thiomorpholinyl-3-pyridazinyl)pyrido[2,3-d]pyrimidine

Prepared as described for Example 367 except substituting thiomorpholine for (1S,4S)-2-aza-5-oxa-bicyclo[2.2.1]heptane.

IR (microscope) 3426, 3063, 1605, 1556, 1442, 1377, 1265 cm^{-1} ; MS m/z 481 (M+H)⁺.

5

Example 603

4-amino-5-(3-bromophenyl)-7-(6-(2,5-dihydropyrrrol-3-yl)pyrido[2,3-d]pyrimidine

Prepared according to the procedure of Example 306.

IR (microscope) 3468, 3060, 1607, 1550, 1443, 1265 cm^{-1} ; MS m/z 446 (M+H)⁺.

10

Example 604

4-amino-5-(3-bromophenyl)-7-(6-(1,3-dioxa-8-azaspiro[4.5]decan-8-yl)-3-pyridyl)pyrido[2,3-d]pyrimidine

Prepared according to the procedure in Example 346, with potassium-t-butoxide and dibromomethane in dimethylformamide.

15

IR (microscope) 3468, 3052, 1557, 1509, 1407, 1289 cm^{-1} ; MS m/z 520 (M+H)⁺.

Example 605

4-amino-5-(3-bromophenyl)-7-(6-hydroxy-3-pyridazinyl)pyrido[2,3-d]pyrimidine

Prepared according to the procedure of Example 246c substituting thiomorpholine for dimethylamine.

IR(KBr) 3487, 1601, 1562, 1502, 1128 cm^{-1}

MS m/z 481 (M+H)⁺

Example 606

25

4-amino-5-(2,3-dichlorophenyl)-7-(6-(1,4-dioxa-8-azaspiro[4.5]decan-8-yl)-3-pyridyl)pyrido[2,3-d]pyrimidine

The procedure of Example 392 was followed, except substituting 5-acetyl-2-(1,4-dioxa-8-azaspiro[4.5]decan-8-yl)pyridine for 5-acetyl-2-morpholinylpyridine. Treatment with HCl/ethanol to form the hydrochloride salt was omitted, and the free base was obtained instead.

IR (MIC) 3480, 3120, 1635, 1605, 1561, 1515, 1429, 1240cm⁻¹; MS m/z 507 (M-H)⁻

Example 607

4-amino-5-isopropyl-7-(6-(1,4-dioxa-8-azaspiro[4.5]decan-8-yl)-3-pyridyl)pyrido[2,3-d]pyrimidine

Prepared by the method of Example 327, substituting 2-methylpropanal for 3-bromobenzaldehyde.

mp: ~ 205°C;

MS (FAB)⁺ m/z calc'd for C₂₂H₂₇N₆O₂: 407.2195, found: 407.2186.

10 IR (cm⁻¹): 3318, 3142, 2960, 1586, 1554, 1514, 1425, 1344, 1240, 1105.

Example 608 .3

4-amino-5-(3-bromophenyl)-7-(6-piperidinyl-3-pyridyl)pyrido[2,3-d]pyrimidine

The title compound was prepared as described for Example 370 substituting 15 piperidine for 4-methoxypiperidine, followed by treatment with 1M HCl ether
 MS (APCI+) m/z 461 (M+H)⁺;
¹H NMR (300 MHz, DMSO-d₆) δ 10.05 (bs, 1H), 9.00 (m, 1H), 8.90 (s, 1H), 8.70 (m, 1H), 8.23 (m, 1H), 7.82 (m, 1H), 7.60 (m, 2H), 7.40 (m, 2H), 3.87 (m, 4H), 1.68 (m, 6H)

Example 609

4-amino-5-(3-bromophenyl)-7-(6-(3-(4-tetrahydropyranlyoximino)pyrrolidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine

The title compound was prepared as described for Example 370 substituting 3-(4'-tetrahydropyranly-oximino)pyrrolidine (prepared as in A-321236.3) for 4-methoxypiperidine, followed by treatment with 1M HCl ether.
 MS (ESI+) m/z 560 (M+H)⁺;
¹H NMR (300 MHz, DMSO-d₆) δ 10.00 (bs, 1H), 9.14 (s, 1H), 8.90 (s, 1H), 8.65 (m, 1H), 7.97 (s, 1H), 7.82 (m, 1H), 7.60 (m, 2H), 7.38 (m, 1H), 7.04 (m, 1H) 4.39 (m, 2H), 4.25 (m, 1H), 3.84 (m, 4H), 3.42 (m, 2H), 2.94 (m, 2H), 1.94 (m, 2H), 1.57 (m, 2H)

30

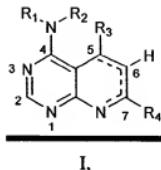
Example 610 4-amino-5-(2-trifluorophenylphenyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine

Prepared as described for Example 395 except substituting 2-trifluoromethylbenzaldehyde for 2,5-dichlorobenzaldehyde.

5 IR (KBr) 3495, 1674, 1634, 1487, 1421, 1321, 1302, 1190cm⁻¹;
MS m/z 452.9 (M+H)⁺.

WHAT IS CLAIMED IS:

1. A method of inhibiting adenosine kinase by administering to a mammal in need of such treatment a pharmaceutically effective amount of one or more compounds of formula I



or a pharmaceutically acceptable salt or amide thereof in vitro or to a mammal wherein,

R¹ and R² are each independently selected from the group consisting of hydrogen, 10 alkenyl, alkoxyalkyl, alkoxyalkylcarbonyl, alkoxy carbonyl, alkoxy carbonylalkyl, alkyl, alkylcarbonyl, aminocarbonyl, aryl, arylalkyl, arylalkylcarbonyl, arylcarbonyl, carboxyalkyl, formyl, haloalkylcarbonyl, heterocycle, heterocyclealkyl, heterocyclecarbonyl, hydroxyalkyl, iminoalkyl, and (NZ₁Z₂)alkyl, or R¹ and R² may join together with the nitrogen atom to which they are attached to form a 5-7 membered ring 15 optionally containing 1-2 additional heteroatoms selected from the group consisting of O, N, and S;

Z₁ and Z₂ are each independently selected from the group consisting of hydrogen, alkoxy carbonyl, alkyl, alkylcarbonyl, benzyl, benzyloxycarbonyl, and formyl;

20 R³ is selected from the group consisting of alkenyl, alkyl, alkynyl, aryl, arylalkyl, cycloalkyl, cycloalkylalkyl, heterocycle, heterocyclealkyl, heterocyclealkylcarbonyl, (NZ₁Z₂)alkyl, and -R^AR^B;

R^A is selected from the group consisting aryl and arylalkyl;

R^B is selected from the group consisting of aryl, arylalkoxy, arylalkyl, aryloxy, 25 heterocycle, and heterocyclealkyl;

R⁴ is selected from the group consisting of alkenyl, alkoxyalkynyl, alkyl, alkynyl, cycloalkyl, aryl, arylalkyl, heterocycle, heterocyclealkyl, and -R^CR^DR^E;

R^C is selected from the group consisting of aryl, arylalkyl, heterocycle, and heterocyclealkyl;

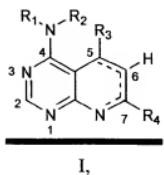
R^D is selected from the group consisting of aryl, arylalkoxy, arylalkoxyimino, arylalkyl, aryloxy, heterocycle, heterocyclealkoxy, heterocyclealkyl, heterocyclecarbonyl, 5 heterocycleimino, heterocycleoxy, heterocycleoxyalkyl, heterocleoxyimino, heterocleoxyiminoalkyl, and heterocyclesulfonyl;

R^E is absent or selected from the group consisting of aryl, arylalkoxy, arylalkoxyimino, arylalkyl, aryloxy, heterocycle, heterocyclealkoxy, heterocyclealkyl, heterocyclecarbonyl, heterocycleimino, heterocycleoxy, heterocycleoxyalkyl, 10 heterocleoxyimino, heterocleoxyiminoalkyl, and heterocyclesulfonyl; and a dashed line --- indicates that a double bond is optionally present provided that proper valencies are maintained;

with the proviso that the following compounds are excluded,

4-amino-5-(4-chorophenyl)-7-(4-nitrophenyl)pyridol[2,3-d]pyrimidine,
 15 4-amino-5-(4-methoxyphenyl)-7-(4-nitrophenyl)pyridol[2,3-d]pyrimidine,
 4-amino-5-(4-fluorophenyl)-7-(4-fluorophenyl)pyridol[2,3-d]pyrimidine,
 4-amino-5-(4-chlorophenyl)-7-(4-fluorophenyl)pyridol[2,3-d]pyrimidine,
 4-amino-5-phenyl-7-(4-aminophenyl)pyrido[2,3-d]pyrimidine,
 4-amino-5-phenyl-7-(4-bromophenyl)pyrido[2,3-d]pyrimidine,
 20 4-amino-5-(4-methoxyphenyl)-7-(4-aminophenyl)pyrido[2,3-d]pyrimidine,
 4-amino-5-(4-methoxyphenyl)-7-(4-bromophenyl)pyrido[2,3-d]pyrimidine, and
 4-amino-5,7-diphenylpyrido[2,3-d]pyrimidine.

2. A method of inhibiting adenosine kinase according to claim 1 comprising
 25 administering a compound of formula I

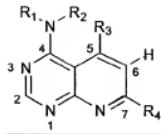


or a pharmaceutically acceptable salt or amide thereof wherein,

R¹ and R² are each independently selected from the group consisting of hydrogen, alkenyl, alkoxyalkyl, alkoxyalkylcarbonyl, alkoxy carbonyl, alkyl, alkyl carbonyl, aminocarbonyl, aryl, aryl carbonyl, carboxyalkyl, formyl, haloalkyl carbonyl,
5 heterocycle alkyl, hydroxyalkyl, iminoalkyl, and (NZ₁Z₂)alkyl, or R¹ and R² may join together with the nitrogen atom to which they are attached to form a 6 membered ring optionally containing 1 additional heteroatom selected from the group consisting of O, N, and S;

R³ is selected from the group consisting of alkenyl, alkyl, aryl, arylalkyl,
10 cycloalkyl, heterocycle, heterocycle alkyl, (NZ₁Z₂)alkyl, and -R^AR^B;
R^A is selected from the group consisting of aryl and arylalkyl;
R^B is selected from the group consisting of aryl, arylalkoxy, arylalkyl, aryloxy, and heterocycle;
R⁴ is selected from the group consisting of alkoxyalkynyl, alkynyl, aryl,
15 heterocycle, and -R^CR^DR^E;
R^C is selected from the group consisting of aryl and heterocycle;
R^D is selected from the group consisting of aryl, arylalkoxy, arylalkyl, aryloxy, heterocycle, heterocycle alkoxyl, heterocycle alkyl, heterocycle carbonyl, heterocycle oxyl, and heterocyclesulfonyl;
20 R^E is absent or selected from the group consisting of aryl, arylalkoxy, arylalkoxyimino, arylalkyl, aryloxy, heterocycle, heterocycle alkoxyl, heterocycle alkyl, heterocycle carbonyl, heterocycle imino, heterocycle oxyl, heterocycle oxylalkyl, heterocycle oxylimino, and heterocycle oxyliminoalkyl;
Z₁ and Z₂ are each independently selected from the group consisting of hydrogen,
25 alkoxy carbonyl, alkyl, alkyl carbonyl, benzyl, benzyloxy carbonyl, and formyl; and
a dashed line --- indicates that a double bond is optionally present provided that proper valencies are maintained.

3. A method of inhibiting adenosine kinase according to claim 1 comprising
30 administering a compound of formula II



II,

or a pharmaceutically acceptable salt or amide thereof wherein,

R¹ and R² are each independently selected from the group consisting of hydrogen, 5 alkenyl, alkoxyalkyl, alkoxyalkylcarbonyl, alkoxy carbonyl, alkyl, alkyl carbonyl, aminocarbonyl, aryl, aryl carbonyl, carboxyalkyl, formyl, haloalkylcarbonyl, heterocyclealkyl, hydroxyalkyl, iminoalkyl, and (N₁Z₂)alkyl, or R¹ and R² may join together with the nitrogen atom to which they are attached to form a 6 membered ring optionally containing 1 additional heteroatom selected from the group consisting of O, N, 10 and S;

R³ is selected from the group consisting of alkenyl, alkyl, aryl, arylalkyl, cycloalkyl, heterocycle, heterocyclealkyl, (N₁Z₂)alkyl, and -R^AR^B;

R^A is selected from the group consisting of aryl and arylalkyl;

R^B is selected from the group consisting of aryl, arylalkoxy, arylalkyl, aryloxy, and 15 heterocycle;

R⁴ is selected from the group consisting of alkoxyalkynyl, alkynyl, aryl, heterocycle, and -R^CR^DR^E;

R^C is selected from the group consisting of aryl and heterocycle;

R^D is selected from the group consisting of aryl, arylalkoxy, arylalkyl, aryloxy, 20 heterocycle, heterocyclealkoxy, heterocyclealkyl, heterocyclecarbonyl, heterocycleoxy, and heterocyclesulfonyl;

R^E is absent or selected from the group consisting of aryl, arylalkoxy, arylalkoxyimino, arylalkyl, aryloxy, heterocycle, heterocyclealkoxy, heterocyclealkyl, heterocyclecarbonyl, heterocycleimino, heterocycleoxy, heterocleoxyalkyl, 25 heterocycleoxyimino, and heterocycleoxyiminoalkyl; and,

Z₁ and Z₂ are each independently selected from the group consisting of hydrogen, alkoxy carbonyl, alkyl, alkyl carbonyl, benzyl, benzyloxy carbonyl, and formyl.

4. The method according to claim 3 wherein R⁴ is selected from the group consisting of:

phenyl; thiophene-2-yl; 3-methyl-2-oxobenzoxazolin-6-yl; 2-(dimethylamino)-5-pyrimidinyl; 2-(N-formyl-N-methyl amino)-5-pyrimidinyl; 2-(N-methoxyethyl-N-methyl amino)-5-pyrimidinyl; 2-(N-methylamino)-5-pyrimidinyl; 2-(1-morpholinyl)-5-pyrimidinyl; 2-(1-pyrrolidinyl)-5-pyrimidinyl; 2-dimethylamino-5-pyrimidinyl; 2-furanyl; 2-oxobenzoxazolin-6-yl; 2-pyridyl; 3-(dimethylamino)phenyl; 3-amino-4-methoxyphenyl; 3-bromo-4-(dimethylamino)phenyl; 3-methoxyphenyl; 3-methyl-4-(N-acetyl-N-methylamino)phenyl; 3-methyl-4-(N-methyl-N-(trifluoroacetyl)amino)phenyl; 3-methyl-4-(N-methylamino)phenyl; 3-methyl-4-pyrrolidinylphenyl; 3-pyridyl; 3,4-dichlorophenyl; 3,4-methylenedioxyphenyl; 3,4,5-trimethoxyphenyl; 4-(acetylamino)phenyl; 4-(dimethylamino)-3-fluorophenyl; 4-(dimethylamino)phenyl; 4-(imidazol-1-yl)phenyl; 4-(methylthio)phenyl; 4-(morpholinyl)phenyl; 4-(N-(2-dimethylamino)ethyl)amino)phenyl; 4-(N-(2-methoxyethyl)amino)phenyl; 4-(N-acetyl-N-methylamino)phenyl; 4-(N-ethyl-N-formylamino)phenyl; 4-(N-ethylamino)phenyl; 4-(N-formyl-N-(2-methoxyethyl)amino)phenyl; 4-(N-isopropylamino)phenyl; 4-(N-methyl-N-(2-dimethylamino)ethyl)amino)phenyl; 4-(N-methyl-N-(2-N-phthalimidyl)acetyl)amino)phenyl; 4-(N-methyl-N-(2-cyano)ethylamino)phenyl; 4-(N-methyl-N-(2-methoxyethyl)amino)phenyl; 4-(N-methyl-N-(3-methoxy)propionylamino)phenyl; 4-(N-methyl-N-acetylamino)phenyl; 4-(N-methyl-N-formylamino)phenyl; 4-(N-methyl-N-trifluoroacetyl)amino)phenyl; 4-(N-morpholinyl)phenyl; 4-(thiophene-2-yl)phenyl; 4-(ureido)phenyl; 4-(2-dimethylamino)acetyl)amino)phenyl; 4-(2-methoxy)acetyl)amino)ethyl)amino)phenyl; 4-(2-methoxy)ethoxyphenyl; 4-(2-oxo-3-oxazolidinyl)phenyl; 4-(4-methoxy-2-butyl)phenyl; 4-(4-methylpiperidinyl)phenyl; 4-(5-pyrimidinyl)phenyl; 4-aminophenyl; 4-bromophenyl; 4-butoxyphenyl; 4-carboxamidophenyl; 4-chlorophenyl; 4-cyanophenyl; 4-diethylaminophenyl; 4-diethylmalonylallylphenyl; 4-dimethylaminophenyl; 4-ethoxyphenyl; 4-ethylphenyl; 4-fluorophenyl; 4-hydroxyphenyl; 4-imidazolylphenyl; 4-

iodophenyl; 4-isopropylphenyl; 4-methoxyphenyl; 4-methylaminophenyl; 4-methylsulfonylphenyl; 4-morpholinylphenyl; 4-N-(2-(dimethylamino)ethyl)-N-formylamino)phenyl; 4-N-(3-methoxypropionyl)-N-isopropyl-amino)phenyl; 4-N-ethyl-N-(2-methoxyethyl)amino)phenyl; 4-N-formylpiperazinylphenyl) 4-nitrophenyl; 4-piperidinylphenyl; 4-(3-pyridyl)phenyl; 4-pyrrolidinylphenyl; 4-t-butylacrylphenyl; 5-(dimethylamino)thiophene-2-yl; 5-amino-2-pyridyl; 5-dimethylamino-2-pyrazinyl; 3-dimethylaminopyridazin-6-yl; 5-dimethylamino-2-pyridyl; 5-pyrimidinylphenyl; 6-(N-methyl-N-formylamino)-3-pyridinyl; 6-(N-methyl-N-methoxyethylamino)-3-pyridinyl; 6-(2-oxo-3-oxazolidinyl)-3-pyridinyl; 6-dimethylamino-3-pyridinyl; 6-imidazolyl-3-pyridinyl; 6-morpholinyl-3-pyridinyl; 6-pyrrolidinyl-3-pyridinyl; 6-(2-propyl)-3-pyridinyl; (4-formylamino)phenyl; 6-(4-oxopiperidinyl)-3-pyridazinyl; 6-(4-morpholinylminopiperidinyl)-3-pyridazinyl; 6-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptan-5-yl)-3-pyridazinyl; 6-(4-methoxyiminopiperidinyl)-3-pyridazinyl; 6-phenylmethoxy-3-pyridazinyl; 6-(1,1-dioxidothiazolidin-3-yl)-3-pyridyl; 6-(1,3-dioxa-8-azaspiro[4.5]decan-8-yl)-3-pyridyl; 6-(1-oxa-4-thia-8-azaspiro[4.5]decan-8-yl)-3-pyridyl; 6-(1,1-dioxidothiomorpholinyl)-3-pyridazinyl; 6-(1-oxa-4,4-dioxido-4-thia-8-azaspiro[4.5]decan-8-yl)-3-pyridyl; 6-(1-oxa-4-oxo-4-thia-8-azaspiro[4.5]decan-8-yl)-3-pyridyl; 6-(3-hydroxy-8-azabicyclo[3.2.1]octan-8-yl)-3-pyridyl; 6-(4-oxo-1-phenyl-1,3,8-triazaspiro[4.5]decan-8-yl)-3-pyridyl; 6-(4-oxo-1-phenyl-1,3,8-triazaspiro[4.5]decan-8-yl)-3-pyridyl; 6-(N-1,4-dioxa-8-azaspiro[4.5]decan-8-yl)-3-pyridylsulfonamide; 2-(1,1-dioxidothiomorpholinyl)-5-thiazoyl; 5-(1,4-dioxa-8-azaspiro[4.5]decan-8-yl)-2-pyrazinyl; 2-(1,4-dioxa-8-azaspiro[4.5]decan-8-yl)-5-thiazoyl; 6-(hexahydro-1H-furo[3,4-c]pyrrol-5-yl)-3-pyridazinyl; 6-(hexahydro-1H-furo[3,4-c]pyrrol-5-yl)-3-pyridyl; 6-(4,7-epoxy-7-methyl-2,3,3A,4,5,6,7,7a-octahydro-1H-isoindolyl)-3-pyridazinyl; 6-(4-(4-tetrahydropyranloxy)iminopiperidinyl)-3-pyridazinyl; 6-isopropoxy-3-pyridazinyl; 6-(2,4-dioxo-(1H,3H)-quinazolin-3-yl)-3-pyridyl; 6-(4-(N-methylpiperazinyl)iminopiperidinyl)-3-pyridazinyl; 6-(4-tetrahydropyranloxy)-3-pyridazinyl; 6-morpholinylethoxy-3-pyridazinyl; 6-(4-ethoxypiperidinyl)-3-pyridazinyl; 6-(1,4-dioxa-8-azaspiro[4.5]decan-8-yl)-3-pyridyl; 6-(4-(2-ethoxyethoxy)piperidinyl)-3-pyridazinyl; 6-((3aR,6aS)-2-oxo-tetrahydro-3aH-[1,3]dioxolo[4,5-c]pyrrol-5-yl)-3-pyridyl;

6-(4-(4-tetrapyranyloxyethyl)piperidinyl)-3-pyridazinyl; 6-(3-(R)-tetrahydrofuranloxy)piperidinyl)-3-pyridazinyl; 6-(3-(S)-tetrahydrofuranloxy)piperidinyl)-3-pyridazinyl; 6-(trans-3-ethoxy-4-hydroxy)pyrrolidinyl)-3-pyridazinyl; 6-(cis-3-ethoxy-4-hydroxy)pyrrolidinyl)-3-pyridazinyl; 6-(trans-3-ethoxy-4-hydroxy)pyrrolidinyl)-3-pyridyl; 6-(trans-3,4-bis-ethoxy)pyrrolidinyl)-3-pyridazinyl; 6-(trans-3,4-bis-ethoxy)pyrrolidinyl)-3-pyridyl; 6-(cis-3,4-bis-ethoxy)pyrrolidinyl)-3-pyridazinyl; 6-(cis-3-amino-4-hydroxy)pyrrolidinyl)-3-pyridyl; 6-(cis-3-amino-4-hydroxy)pyrrolidinyl)-3-pyridazinyl; 6-(cis-3-amino-4-hydroxy)pyrrolidinyl)-3-pyridyl; 6-(1,5-dioxa-9-azaspiro[5.5]undecan-9-yl)-3-pyridazinyl; 6-(4-tertbutyl)piperidinyl-3-pyridazinyl; 6-(4-N-formyl)piperidinyl-3-pyridazinyl; 6-morpholinyl-3-pyridazinyl; 4-N-1,4-dioxa-8-azaspiro[4.5]decan-8-ylbenzenesulfonamide; 4-(4-dioxa-8-azaspiro[4.5]decan-8-ylcarboxamide)phenyl; 6-(3-methoxy-1,5-dioxa-9-azaspiro[5.5]undecan-9-yl)-3-pyridazinyl; 6-(1,5-dioxa-3-hydroxymethyl-9-azaspiro[5.5]undecan-9-yl)-3-pyridazinyl; 6-(S-O-ethyl-2-hydroxymethylpyrrolidinyl)-3-pyridazinyl; 6-(4-acetyl-1-oxa-4,8-diazaspiro[4.5]decan-8-yl)-3-pyridazinyl; 6-(2R,3R)-2,3-bis(methoxymethyl)-1,4-dioxa-8-azaspiro[4.5]decan-8-yl)-3-pyridazinyl; 6-(2S,3S)-2,3-dimethyl-1,4-dioxa-8-azaspiro[4.5]decan-8-yl)-3-pyridazinyl; 6-(4,4-(cis-1,2-dioxy)cyclopentane)piperidinyl)-3-pyridazinyl; 6-(4,4-(1S,2S-dimethoxymethylethanedioxy)piperidinyl)-3-pyridazinyl; 6-(4,4-(cis-3,4-dioxy-oxacyclopentane)piperidinyl)-3-pyridazinyl; 6-(4,4-(1,3-dioxy-2-methoxypylene)piperidinyl)-3-pyridazinyl; 6-(4,4-(1,3-dioxy-2-hydroxymethylpropylene)piperidinyl)-3-pyridazinyl; 6-(4,4-(2-(2,2-spiro-oxacyclopropane-1,3-dioxypropylene)piperidinyl)-3-pyridazinyl; 6-morpholinyl-3-pyridazinyl; 6-(4-morpholinyliminopiperidinyl)-3-pyridyl; 6-(4-(N-methylpiperazinyl)iminopiperidinyl)-3-pyridyl; 6-(4-(1,2,4-triazol-1-yl)iminopiperidinyl)-3-pyridyl; 6-(4-ethylpiperidinylcarboxylate)-3-pyridyl; 2-phenylmethyl-3(2H)-pyridazinone-6-yl; 6-(4-(morpholinylcarboxamide)piperidinyl)-3-pyridyl; 6-(4-(N-morpholinylaminocarboxamide)piperidinyl)-3-pyridyl; 6-(4-(N,N-dimethylaminocarboxamide)piperidinyl)-3-pyridyl; 6-(4-(N-methyl-N-

methoxyethylcarboxamide)piperidinyl)-3-pyridyl; 6-(4-(N-methoxyethylcarboxamide)piperidinyl)-3-pyridyl; 6-(4-hydroxymethylpiperidinyl)-3-pyridyl; 6-(4-hydroxypiperidinyl)-3-pyridyl; 6-(4-N-acetyl piperazinyl)-3-pyridyl; 6-(4-cyanopiperidinyl)-3-pyridyl; 6-(4-N-(4-fluorophenyl)piperazinyl)-3-pyridyl; 4-5 morpholinylbenzenesulfonamide; 4-N-4,4-ethylenedioxypiperidinylbenzenesulfonamide; 4-N-cyclopropylbenzenesulfonamide; 4-piperidinebenzenesulfonamide; 4-(4-cyanopiperidine)benzenesulfonamide; 4-N-cyclopropylmethylbenzenesulfonamide; 4-N,N-dimethylaminobenzenesulfonamide; 4-N-(S)-2-hydroxymethylpyrrolidinebenzenesulfonamide; 4-(4-10 hydroxypiperidine)benzenesulfonamide; 4-(cis-3,5-dimethylmorpholinyl)benzenesulfonamide; 3-fluoro-4-thiomorpholinylphenyl; 6-(thiomorpholinyl)-3-pyridyl; 6-(4,4-dioxothiomorpholinyl)-3-pyridyl; 4-(4,4-ethylenedioxypiperidinylcarboxamide)phenyl; 4-(N-cyclopropylcarboxamide)phenyl; 4-(morpholinylcarboxamide)phenyl; 6-N-cyclopropylamino-3-pyridyl; 4-(4-15 hydroxypiperidinylcarboxamide)phenyl; 6-(S)-hydroxymethylpyrrolidinyl-3-pyridazinyl; 6-(4-(2-ethoxyethoxy)piperidinyl)-3-pyridyl; 6-hexahydropryrimidine)-3-pyridyl; 6-(S)-2-ethoxyethoxypyrrolidinyl)-3-pyridyl; 6-(R)-2-ethoxyethoxypyrrolidinyl)-3-pyridyl; 6-(cis-3,4-dihydroxypyroolidinyl)-3-pyridyl; 6-[(3aR,6aS)-tetrahydro-3aH-[1,3]dioxolo[4,5-c]pyrrol-2-one-5-yl]-3-pyridyl; 6-(cis-2,3-dihydroxypyroolidinyl)-3-pyridazinyl; 6-(S,R)-2-20 hydroxymethyl-4-hydroxypyroolidinyl)-3-pyridyl; 6-(R-2-hydroxymethyl-4-pyrrolidinyl)-3-pyridazinyl; 6-(1S,4S)-2-aza-5-oxa-bicyclo[2.2.1]heptane)-3-pyridyl; 6-(2-imidizolidone-1-yl)-3-pyridyl; 4-(2,4-(1H,3H)-quinazolinedion-3-yl)phenyl; 6-morpholinylcarboxamide-3-pyridazinyl; 6-methoxy-3-pyridazinyl; 6-N,N-dethoxyethylamino-3-pyridazinyl; 6-(4-ethoxymethylpiperidinyl)-3-pyridazinyl; 6-(4-(4-25 tetrahydropyranylmethyl)piperidinyl)-3-pyridazinyl; 6-(4-ethoxyethoxymethylpiperidinyl)-3-pyridazinyl; 6-N-methyl-N-1,3-dioxalanemethylamino)-3-pyridazinyl; 6-(4,4-dioxyethylenecyclohexyloxy)-3-pyridazinyl; 6-dihydroxymethylmethoxy-3-pyridazinyl; 6-(3-pyridyloxy)-3-pyridazinyl; 4,7-epoxy-7-methyl-2,3,3A,4,5,6,7,7a-octahydro-1H-isoindolyl; 6-(4-N-methyl-N-methoxyethyl)-3-pyridazinyl; 6-(3,4-dimethoxymethoxypyrrolidinyl)-3-pyridazinyl; 6-(trans-3-hydroxy-4-30

5 methylpyrrolidinyl)-3-pyridazinyl; 6-(trans-3-hydroxy-4-methylpyrrolidinyl)-3-pyridyl; 6-(cis-3-hydroxy-4-methylpyrrolidinyl)-3-pyridazinyl; 6-(cis-3-hydroxy-4-methylpyrrolidinyl)-3-pyridyl; 6-(trans-3-cyano-4-hydroxypyrrrolidinyl)-3-pyridyl; 6-(3-hydroxy-4-tert-butylcarboxamidepyrrolidinyl)-3-pyridyl; 6-(S-2-(4-tetrahydropyranloxy)methylpyrrolidinyl)-3-pyridazinyl; 6-(2-(4-tetrahydropyranloxy)iminopyrrolidinyl)-3-pyridazinyl; 2-morpholinyl-5-thiazoyl; 5-bromo-2-thienyl; 2,5-dimethyl-3-thienyl; 5-chloro-2-thienyl; 2,4-dimethyl-5-thiazoyl; 5-methyl-2-thienyl; 2-furanyl; 2-(4,4-dioxoethylenepiperidinyl)-5-thiazoyl; 3-thienyl; 3-methyl-2-thienyl; 2-morpholinyl-4-thiazoyl; 2-morpholinyl-4-trifluoromethyl-5-thiazoyl;

10 5-morpholinyl-2-thienyl; 4-methyl-2-morpholinyl-5-thiazoyl; 2,5-dichloro-3-thienyl; 2,5-dimethyl-3-furanyl; N-methyl-2-pyrrolyl; 2-N,N-dimethylamino-5-thiazoyl; 2-morpholinyl-5-thiazoyl; 2-(4,4-dioxothiomorpholinyl)-5-thiazoyl; 1-N-methyl-2-morpholinyl-5-imidazoyl; 2-morpholinyl-5-oxazolyl; 2-N-methyl-N-methoxyethylamino-5-thiazoyl; 2-N-methyl-N-ethylamino-5-thiazoyl; 2-N-pyrrolidinyl-5-thiazoyl; 2-N-methyl-N-propylamino-5-thiazoyl; 2-N,N-diethylamino-5-thiazoyl; 2-(N-methylpiperazinyl)-5-thiazoyl; 2-(N-(2-pyridyl)piperazinyl)-5-thiazoyl; 2-N-methy-N-(2-pyridylethyl)-5-thiazoyl; 2-(4-oxopiperazinyl)-5-thiazoyl; 2-(4-(N-morpholinyl)iminopiperazinyl)-5-thiazoyl; 6-N-morpholine-3-pyridinesulfonamide; 2-(4-oxopiperidinyl)-5-pyrimidyl; 2-(4,4-dioxethylenepiperidinyl)-5-pyrimidyl; 5-(4,4-dioxethylenepiperidinyl)-2-pyrazinyl; 5-(4-oxopiperidinyl)-2-pyrazinyl; 6-N-cyclopropyl-3-pyridinesulfonamide; 6-N-(4,4-dioxethylenepiperidinyl)-3-pyridinesulfonamide; 2-(4-(4-tetrahydropyranloxy)iminopiperidinyl)-5-pyrazinyl; 6-(4-(phenylmethoxy)iminopiperidinyl)-3-pyridyl; 6-(4-(tert-butyloxy)iminopiperidinyl)-3-pyridyl; 6-(4-(cyclohexyloxy)iminopiperidinyl)-3-pyridyl; 6-(4-hydroxyiminopiperidinyl)-3-pyridyl; 6-(4-(4-tetrahydropyranloxy)iminopiperidinyl)-3-pyridyl; 6-(4-methoxyethoxyiminopiperidinyl)-3-pyridyl; 6-(4-(2-thenylmethoxy)iminopiperidinyl)-3-pyridyl; 6-(4-(1-(4-tetrahydropyranloxy)iminoethyl)-4-hydroxypiperidinyl)-3-pyridazinyl; 6-(4-(1-(4'-acetyl-4'-hydroxypiperidinyl)-3-pyridazinyl; 6-(4-(1-(isopropylcaboxymethoxy)iminoethyl))-4-hydroxypiperidinyl)-3-pyridyl; 6-(4-(1-(ethylcaboxymethoxy)iminoethyl))-4-hydroxypiperidinyl)-3-pyridyl; 6-(4-(1-(ethylcaboxymethoxy)iminoethyl))-4-

hydroxypiperidinyl)-3-pyridyl; 6-(4-(1-(methylcaboxymethoxy)iminoethyl))-4-hydroxypiperidinyl)-3-pyridyl; 6-(4-(1-(2-tetrahydropyranlyloxy)iminoethyl))-4-hydroxypiperidinyl)-3-pyridyl; 6-(4-(1-allyloxy)iminoethyl))-4-hydroxypiperidinyl)-3-pyridyl; 6-(4-(1-ethoxy)iminoethyl))-4-hydroxypiperidinyl)-3-pyridyl; 6-(4-(1-methoxy)iminoethyl))-4-hydroxypiperidinyl)-3-pyridyl; 6-(4-(1-hydroxy)iminoethyl))-4-hydroxypiperidinyl)-3-pyridyl; 6-(4-(2-tetrahydropyranlyoxy)iminopiperidinyl)-3-pyridyl; 6-(4-(isopropylcarboxymethoxy)iminopiperidinyl)-3-pyridyl; 6-(4-hydroxy-4-(1-(4-tetrahydropyranlyloxy)iminoethyl))-4-hydroxypiperidinyl)-3-pyridyl; 6-(4-(3-butylolactone)-4-hydroxypiperidinyl)-3-pyridyl; 6-(4-(2-butylolactone))-4-hydroxypiperidinyl)-3-pyridyl; 6-(4-(3-hydroxyazetidinyl)-3-pyridyl; 6-(cis-3-hydroxytropanyl)-3-pyridyl; 6-(cis-2,3-dihydroxypiperidinyl)-3-pyridyl; 6-(N-methyl-N-(3-pyridylmethyl)amino)-3-pyridazinyl; 6-(1,2,3,6-tetrahydropyridyl)-3-pyridyl; 6-(4-(N,N'-methoxyphenylcarbamoyl)piperidinyl)-3-pyridazinyl; 6-(4-(2-butylolactone)-4-hydroxypiperidinyl)-3-pyridyl; 6-(trans-3,4-bis(N-4'-methoxyphenylcarbamoyl)pyrrolidinyl)-3-pyridyl; 6-(trans-3-hydroxytropanyl)-3-pyridyl; 6-(S,S-trans-3,4-dihydroxypyrrolidinyl)-3-pyridyl; 6-(R,R-trans-3,4-dihydroxypyrrolidinyl)-3-pyridazinyl; 6-(R,R-trans-3,4-dihydroxypyrrolidinyl)-3-pyridyl; 6-(8-(1-phenyl-1,3,8-triaza-2-spiro[4,5]deceN-4-one)-3-pyridyl; 6-(8-(1-phenyl-1,3,8-triaza-2-spiro[4,5]deceN-4-one)-3-pyridyl; 6-(4-(2-keto-1-benzimidazolinyl)piperidinyl)-3-pyridazinyl; 6-(4-oxothiomorpholinyl)-3-pyridyl; 6-(4-(2-keto-1-benzimidazolinyl)piperidinyl)-3-pyridyl; 6-(N-methyl-N-(2-pyridylethyl)amino)-3-pyridyl; 6-(N-methyl-N-(4-pyridylethyl)amino)-3-pyridyl; 6-N-(3-pyridylmethyl)amino-3-pyridyl; 6-(2-hydroxymethylpiperidinyl)-3-pyridyl; 6-(4-hydroxy-4-(4-bromophenyl)piperidinyl)-3-pyridyl; 6-(4-N-(2-pyridyl)piperazinyl)-3-pyridyl; 6-(4-N-(2-pyridyl)piperazinyl)-3-pyridyl; 6-(4,4-diaceetoxyethylthio)piperidinyl)-3-pyridyl; 6-(N-methyl-N-(3-pyridylmethyl)amino)-3-pyridyl; 6-(4-pyrrolidinylpiperidinyl)-3-pyridyl; 6-(4-N-cyanomethylpiperazinyl)-3-pyridyl; 6-(3-hydroxypyrrolidinyl)-3-pyridyl; 6-(4-methylpiperidinyl)-3-pyridyl; 6-(cis-3,5-dimethylmorpholinyl)-3-pyridyl; 6-(4,4-difluoropipridinyl)-3-pyridyl; 6-(4,4-dioxothiomorpholinyl)-3-pyridazinyl; 6-thiazolidinyl-3-pyridyl; 6-(1,1-dioxothiazolidinyl)-3-pyridyl; 6-thiomorpholinyl-3-

pyridazinyl; 6-(2,5-dihydropyrrrolyl)-3-pyridyl; 6-(hexahydro-1H-furo[3,4-c]pyrrol-5-yl)-3-pyridyl; 6-hydroxy-3-pyridazinyl; 6-piperidinyl-3-pyridyl; and 6-(4-tetrahydropyranloxy)iminopyrrolidinyl-3-pyridyl; 6-morpholinyl-3-pyridyl.

5 5. The method according to claim 3 wherein R³ is selected from the group consisting of:

(thiophene-2-yl)methyl; (thiophene-3-yl)methyl; butyl; cycloheptyl; pentyl; thiophene-2-yl; 1-(3-bromophenyl)ethyl; 2-(N-phenylmethoxycarbonyl)aminophenyl; 2-(3-bromophenyl)ethyl; 2-(3-cyanophenyl)methyl; 2-(4-bromophenyl)ethyl; 2-(5-chloro-2-10 (thiophen-3-yl)phenyl; 2-bromophenyl; 2-furanyl; 2-methylpropyl; 2-phenylethyl; phenylmethyl; 2,3-dimethoxyphenyl; 2,3-methylenedioxypyhenyl; 3-(furan-2-yl)phenyl; 3-(thiophen-2-yl)phenyl; 3-(2-pyridyl)phenyl; 3-(3-methoxybenzyl)phenyl; 2-(3-aminopropynyl)phenylmethyl; 3-benzylloxypyhenyl; 3-bromo-4-fluorophenyl; 3-bromo-5-iodophenyl; 3-bromo-5-methoxyphenyl; 3-bromophenyl; 3-bromophenyl)methyl; 3-15 carboxamidophenyl; 3-chlorophenyl; 3-cyanophenyl; 3-diethylmalonylallylphenyl; 3-dimethylaminophenyl; 3-ethoxyphenyl; 3-fluoro-5-trifluoromethylphenyl; 3-fluorophenyl; 3-hydroxyphenyl; 3-iodophenyl; 3-methoxyethoxyphenyl; 3-methoxyphenyl; 3-methylphenyl; 3-methylsulfonylphenyl; 3-methylthiophenyl; 3-t-butylacrylphenyl; 3-trifluoromethoxyphenyl; 3-trifluoromethylphenyl; 3-vinylpyridinylphenyl; 3-4-20 dichlorophenyl; 3,4-dimethoxyphenyl; 3,4-methylenedioxypyhenyl; 3,4,5-trimethoxyphenyl; 3,5-di(trifluoromethyl)phenyl; 3,5-dibromophenyl; 3,5-dichlorophenyl; 3,5-dimethoxyphenyl; 3,5-dimethylphenyl; 4-(2-propyl)phenyl; 4-(2-propyl)oxyphenyl; 4-benzylloxypyhenyl; 4-bromophenyl; 4-bromothiophene-2-yl; 4-butoxyphenyl; 4-dimethylaminophenyl; 4-fluoro-3-trifluoromethylphenyl; 4-methoxyphenyl; 4-25 neopentylphenyl; 4-phenoxyphenyl; 5-bromothiophene-2-yl; 5-cyclohexyl; 5-cyclopropyl; 5-hexyl; 5-methyl; 5-phenyl; (2-bromo-5-chlorophenyl)methyl; (2-bromophenyl)methyl; (5-chloro-2-(3-methoxyphenyl)phenyl)methyl; 3-bromophenyl; 2-pyridyl; 2-ethoxyphenyl; 5-ethoxyphenyl; 2,5-dichlorophenyl; 2,5-dimethylphenyl; 3-fluorophenyl; 3-trifluoromethylphenyl; 5-trifluoromethylphenyl; 3,5-diclorophenyl; 4-bromo-2-thienyl; 30 3-bromo-2-thienyl; 3-cyanophenyl; 4-tetrahydropyranyl; 3-indolyl; 5-indolyl; 4-quinolyl;

2-bromophenyl; 4-fluorophenyl; 4,4-difluorocyclohexyl; 1,1-dimethyl-3-butenyl; 2,3-dichlorophenyl; isopropyl; and 2-trifluorophenylphenyl.

6. The method according to claim 1 wherein the compound is selected from the group
5 consisting of:

4-(N-(2,3-dihydroxypropyl)amino)-5-(3-bromophenyl)-7-(6-morpholinyl-3-pyridinyl)pyrido[2,3-d]pyrimidine;

4-(N-(3-morpholinylpropyl)amino)-5-(3-bromophenyl)-7-(6-morpholinyl-3-pyridinyl)pyrido[2,3-d]pyrimidine;

10 4-(N-(2-(4-imidazolyl)ethyl)amino)-5-(3-bromophenyl)-7-(6-morpholinyl-3-pyridinyl)pyrido[2,3-d]pyrimidine;

4-(N-(3-carboxypropyl)amino)-5-(3-bromophenyl)-7-(6-morpholinyl-3-pyridinyl)pyrido[2,3-d]pyrimidine;

15 (S)-4-amino-5-(3-bromophenyl)-7-(6-(O-methyl-2-hydroxymethylpyrrolidinyl)-3-pyridinyl)pyrido[2,3-d]pyrimidine;

(S)-4-amino-5-(3-bromophenyl)-7-(6-(2-hydroxymethylpyrrolidinyl)-3-pyridinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(2-bromophenyl)-7-(6-(4-hydroxypiperidinyl)-3-pyridinyl)pyrido[2,3-d]pyrimidine;

20 4-amino-5-(4-fluorophenyl)-7-(6-(4,4-ethylenedioxypiperidinyl)-3-pyridinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(2-bromophenyl)-7-(6-(4-hydroxypiperidinyl)-3-pyridazyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4,4-ethylenedioxypiperidinyl)-3-pyridazyl)pyrido[2,3-d]pyrimidine;

25 4-amino-5-(3-bromophenyl)-7-(2-morpholinyl-4-thiazolyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(N-methyl-3-indolyl)-7-(6-morpholinyl-3-pyridinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-ethoxyiminopiperidinyl)-3-pyridinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-ethoxycarbonylmethoxyiminopiperidinyl)-3-pyridinyl)pyrido[2,3-d]pyrimidine;

5 4-amino-5-(4-dimethylaminophenyl)-7-(4-bromophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(4-dimethylaminophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(4-methoxyphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

10 4-amino-5-(4-dimethylaminophenyl)-7-(4-methoxyphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(4-(2-propyl)phenyl)-7-(4-methoxyphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(4-neopentylphenyl)-7-(4-methoxyphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(4-butyloxyphenyl)-7-(4-methoxyphenyl)pyrido[2,3-d]pyrimidine;

15 4-amino-5-(4-methoxyphenyl)-7-(4-bromophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(4-(2-propyl)oxyphenyl)-7-(4-methoxyphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(4-butoxyphenyl)-7-(4-N-formylpiperazinylphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(4-benzyloxyphenyl)-7-(4-methoxyphenyl)pyrido[2,3-d]pyrimidine;

20 4-amino-5-(4-phenoxyphenyl)-7-(4-methoxyphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(4-(2-propyl)phenyl)-7-(4-diethylmalonylallylphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(4-(2-propyl)phenyl)-7-(4-t-butylacylphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

25 4-amino-5-(3,4-dimethoxyphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-t-butylacrylphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-methoxyphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3,5-dimethoxyphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-diethylmalonylallylphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

5 4-amino-5-(3-vinylpyridinylphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-trifluoromethylphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

10 4-amino-5-(3-carboxamidophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-cyanophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-benzyloxyphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

15 4-amino-5-(3-methoxyphenyl)-7-(4-methoxyphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-butoxyphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-(2-pyridyl)phenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

20 4-amino-5-(3-methylphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-chlorophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-fluorophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

25 4-amino-5-(3-bromophenyl)-7-(4-methoxyphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-methoxyphenyl)-7-(4-bromophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-phenylpyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-ethylphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-bromophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-cyanophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-hydroxyphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-iodophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-ethoxyphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-trifluoromethoxyphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3,5-dichlorophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

5 4-amino-5-(3-bromo-4-fluorophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-hydroxyphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-morpholinylphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-piperidinylphenyl)pyrido[2,3-d]pyrimidine;

10 4-amino-5-(3-bromophenyl)-7-(4-imidazol-1-yl)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-chlorophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-isopropylphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-trifluorophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine;

15 4-amino-5-(3-bromophenyl)-7-(3,4,5-trimethoxyphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-(3-methoxybenzyl)phenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-methoxyethoxyphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

20 4-amino-5-(3,4-methylenedioxyphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-ethoxyphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(2'-thiophene)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-fluorophenyl)pyrido[2,3-d]pyrimidine;

25 4-amino-5-(3-dimethylaminophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-phenyl-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3,4,5-trimethoxyphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

30 4-amino-5-(3-bromophenyl)-7-(4-nitrophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-iodophenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3-bromophenyl)-7-(3,4-methylenedioxyphenyl)pyrido[2,3-
5 d]pyrimidine;
4-amino-5-(thiophen-2-yl)-7-(4-morpholinylphenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3,5-dimethoxyphenyl)-7-(thiophen-2-yl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3-bromophenyl)-7-(4-carboxamidophenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3-bromophenyl)-7-(4-(2-methoxyethoxyphenyl)pyrido[2,3-
10 d]pyrimidine;
4-amino-5-(3,5-dimethoxyphenyl)-7-(4-morpholinylphenyl)pyrido[2,3-
d]pyrimidine;
4-amino-5-(3-trifluoromethylphenyl)-7-(thiophene-2-yl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3-bromophenyl)-7-(4-aminophenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3-bromo-4-fluorophenyl)-7-(thiophene-2-yl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3-bromo-4-fluorophenyl)-7-(2-furanyl)pyrido[2,3-d]pyrimidine;
15 4-amino-5-(3,5-dimethoxyphenyl)-7-(4-iodophenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3,5-dimethoxyphenyl)-7-(4-imidazolylphenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3,5-dimethoxyphenyl)-7-(4-(thiophene-2-yl)phenyl)pyrido[2,3-
d]pyrimidine;
4-amino-5-(3,5-dimethoxyphenyl)-7-(4-(3-pyridyl)phenyl)pyrido[2,3-d]pyrimidine;
20 4-amino-5-(3-bromophenyl)-7-(4-(4-methylpiperidinyl)phenyl)pyrido[2,3-
d]pyrimidine;
4-amino-5-(3-bromophenyl)-7-(4-pyrrolidinylphenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(4-bromothiophene-2-yl)-7-(4-dimethylaminophenyl)pyrido[2,3-
d]pyrimidine;
25 4-amino-5-(4-bromothiophene-2-yl)-7-(4-morpholinylphenyl)pyrido[2,3-
d]pyrimidine;
4-morpholinyl-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-
d]pyrimidine;
4-amino-5-(5-bromothiophene-2-yl)-7-(4-morpholinylphenyl)pyrido[2,3-
30 d]pyrimidine;

4-amino-5-(4-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3-bromophenyl)-7-(4-(acetylamino)phenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3,5-dimethoxyphenyl)-7-(5-pyrimidinylphenyl)pyrido[2,3-
5 d]pyrimidine;
4-(4-fluorophenyl)amino-5-(3-bromophenyl)-7-(4-
dimethylaminophenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(4-bromothiophene-2-yl)-7-(4-pyrrolidinylphenyl)pyrido[2,3-
d]pyrimidine;
10 4-amino-5-(4-bromothiophene-2-yl)-7-(thiophene-2-yl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3-bromophenyl)-7-(5-(dimethylamino)thiophene-2-yl)pyrido[2,3-
d]pyrimidine;
4-amino-5-(3-bromo-5-iodophenyl)-7-(4-(dimethylamino)phenyl)pyrido[2,3-
d]pyrimidine;
15 4-amino-5-(3,5-di(trifluoromethyl)phenyl)-7-(4-(dimethylamino)phenyl)pyrido[2,3-
d]pyrimidine;
4-amino-5-(3,5-di(trifluoromethyl)phenyl)-7-(4-morpholinylphenyl)pyrido[2,3-
d]pyrimidine;
4-amino-5-(3,5-dibromophenyl)-7-(4-(dimethylamino)phenyl)pyrido[2,3-
20 d]pyrimidine;
4-amino-5-(3,5-dibromophenyl)-7-(4-morpholinylphenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(4-bromothiophene-2-yl)-7-(4-(4-methylpiperidinyl)phenyl)pyrido[2,3-
d]pyrimidine;
4-amino-5-(3,5-dibromophenyl)-7-(4-(dimethylamino)phenyl)pyrido[2,3-
25 d]pyrimidine;
4-amino-5-(3-bromophenyl)-7-(3-(dimethylamino)phenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3-bromophenyl)-7-(4-methylsulfonylphenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3-bromophenyl)-7-(3-methoxyphenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3-bromophenyl)-7-(4-(methylthio)phenyl)pyrido[2,3-d]pyrimidine;
30 4-amino-5-(3-bromophenyl)-7-(3,4-dichlorophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(N-methyl-N-formylamino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-methylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromo-4-fluorophenyl)-7-(4-methylsulfonylphenyl)pyrido[2,3-d]pyrimidine;

5 4-amino-5-(3-bromophenyl)-7-(3-amino-4-methoxyphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(3-bromo-4-(dimethylamino)phenyl)pyrido[2,3-d]pyrimidine;

10 4-amino-5-(3-bromophenyl)-7-(3-methyl-4-(dimethylamino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(N-methyl-N-trifluoroacetylamino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(dimethylamino)-3-fluorophenyl)pyrido[2,3-d]pyrimidine;

15 4-amino-5-(3-bromophenyl)-7-(4-(N-ethyl-N-formylamino)phenyl)pyrido[2,3-d]pyrimidine;

4,4-bis(acetylamino)-5-(3-bromophenyl)-7-(4-(N-methyl-N-acetylamino)phenyl)pyrido[2,3-d]pyrimidine;

20 4-amino-5-(3-bromophenyl)-7-(4-(N-acetyl-N-methylamino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(N-ethylamino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(N-methyl-N-(2-methoxyethyl)amino)phenyl)pyrido[2,3-d]pyrimidine;

25 4-amino-5-(3-bromophenyl)-7-(4-(N-isopropylamino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-N-ethyl-N-(2-methoxyethyl)amino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-N-(3-methoxypropionyl)-N-isopropyl-30 amino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-N-(2-(dimethylamino)ethyl)-N-formylamino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(N-(2-(dimethylamino)ethyl)amino)phenyl)pyrido[2,3-d]pyrimidine;

5 4-amino-5-(3-bromophenyl)-7-(4-(N-methyl-N-(2-cyano)ethylamino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(N-methyl-N-(3-methoxy)propionylamino)phenyl)pyrido[2,3-d]pyrimidine;

10 4-amino-5-(3-bromophenyl)-7-(3-methyl-4-(N-formyl-N-methylamino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(4-methoxy-2-butyl)phenyl)pyrido[2,3-d]pyrimidine;

15 4-amino-5-(3-bromophenyl)-7-(4-(N-methyl-N-(N-phthalimidyl)acetyl)amino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(3-methyl-4-(N-methyl-N-(trifluoroacetyl)amino)phenyl)pyrido[2,3-d]pyrimidine;

20 4-amino-5-(3-bromophenyl)-7-(3-methyl-4-(N-acetyl-N-methylamino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-dimethylamino-3-pyridinyl)pyrido[2,3-d]pyrimidine;

25 4-amino-5-(3-cyanophenyl)-7-(4-methylsulfonylphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-cyanophenyl)-7-(4-(N-methyl-N-formylamino)-phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(N-methyl-N-formylamino)-3-pyridinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-morpholinyl-3-pyridinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(N-methyl-N-methoxyethylamino)-3-pyridinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-pyrrolidinyl-3-pyridinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(2-(dimethylamino)-5-pyrimidinyl)pyrido[2,3-d]pyrimidine;

5 4-amino-5-(3-bromophenyl)-7-(2-(N-methoxyethyl-N-methyl amino)-5-pyrimidinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(2-(N-formyl-N-methyl amino)-5-pyrimidinyl)pyrido[2,3-d]pyrimidine;

10 4-amino-5-(3-bromophenyl)-7-(2-(N-methylamino)5-pyrimidinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(2-(1-pyrrolidinyl)-5-pyrimidinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(2-(1-morpholiny)-5-pyrimidinyl)pyrido[2,3-d]pyrimidine;

15 4-amino-5-(3-bromophenyl)-7-(6-(2-oxo-3-oxazolidinyl)-3-pyridinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(2-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(3-pyridyl)pyrido[2,3-d]pyrimidine;

20 4-amino-5-(3-(thiophen-2-yl)phenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-(furan-2-yl)phenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-(3-methoxyphenyl)phenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

25 4-amino-5-phenyl-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-chlorophenyl)-7-(4-(morpholiny)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromo-4-fluorophenyl)-7-(4-(morpholiny)phenyl)pyrido[2,3-d]pyrimidine;

30 4-amino-5-(3-chlorophenyl)-7-(4-iodophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-chlorophenyl)-7-(4-(thiophen-2-yl)phenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3-chlorophenyl)-7-(4-(5-pyrimidinyl)phenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3-bromo-4-fluorophenyl)-7-(4-iodophenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(4-bromothiophene-2-yl)-7-(4-methoxyphenyl)pyrido[2,3-d]pyrimidine;
5 4-amino-5-(3-bromophenyl)methyl-7-(4-(dimethylamino)phenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(2-phenylethyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(2-methylpropyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(butyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine;
10 4-amino-5-(2-(4-bromophenyl)ethyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(butyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(2-(3-cyanophenyl)methyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;
15 4-amino-5-(2-(N-phenylmethoxycarbonyl)aminoethyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(cycloheptyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(2-(5-chloro-2-(thiophen-3-yl)phenylmethyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;
20 4-amino-5-(pentyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-hexyl-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(2-(3-bromophenyl)ethyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine;
25 4-amino-5-((2-bromophenyl)methyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-cyclopropyl-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-cyclohexyl-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-((2-bromo-5-chlorophenyl)methyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine;
30 4-amino-5-methyl-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(2,3-methylenedioxyphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-fluoro-5-trifluoromethylphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

5 4-amino-5-(2-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3,5-dimethylphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3,4-dichlorophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

10 4-amino-5-(4-fluoro-3-trifluoromethylphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromo-5-methoxyphenyl)-7-(4-morpholinylphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromo-5-methoxyphenyl)-7-(4-pyrrolidinylphenyl)pyrido[2,3-d]pyrimidine;

15 4-amino-5-(3-bromo-5-methoxyphenyl)-7-(4-piperidinylphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromo-5-methoxyphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-methylthiophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

20 4-amino-5-(3-bromo-5-methoxyphenyl)-7-(thiophene-2-yl)pyrido[2,3-d]pyrimidine;

4-amino-5-(2,3-dimethoxyphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

25 4-amino-5-(3-methylsulfonylphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-acetylamo-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-formylamino-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

30 4-formylamino-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-(methoxycetyl)amino-5-(3-bromophenyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-trifluoroacetylamino-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

5 4-pentanoylamino-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-benzoylamino-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

10 4-(N-BOC-glycyl)amino-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-(N-phthalimidylglycyl)amino-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-(ethoxycarbonyl)amino-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

15 4-(ethylaminocarbonyl)amino-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-allylamino-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-(2-(N,N-dimethylamino)ethylamino)-5-(4-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

20 4-(4-(N,N-dimethylamino)butylamino)-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-(N-allyl-N-formylamino)-5-(4-dimethylaminophenyl)-7-(4-bromophenyl)pyrido[2,3-d]pyrimidine;

25 4-diacetylamino-5-(p-dimethylaminophenyl)-7-(4-bromophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(5-amino-2-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(5-dimethylamino-2-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(5-dimethylamino-2-pyrazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(2-oxobenzoxazolin-6-yl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(1-methyl-2-oxobenzoxazolin-6-yl)pyrido[2,3-d]pyrimidine;

5 4-amino-5-((5-chloro-2-(3-methoxyphenyl)phenyl)methyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-((thiophene-2-yl)methyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine;

10 4-amino-5-((thiophene-3-yl)methyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-((2-bromophenyl)methyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(N-formyl-N-(2-methoxyethyl)amino)phenyl)pyrido[2,3-d]pyrimidine;

15 4-amino-5-(3-bromophenyl)-7-(4-(N-(2-methoxyethyl)amino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(N-methyl-N-((2-dimethylamino)ethyl)amino)phenyl)pyrido[2,3-d]pyrimidine;

20 4-amino-5-(3-bromophenyl)-7-(4-(2-methoxy)acetylamino)ethyl)amino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-((4-formylamino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(2-dimethylamino)acetylamino)phenyl)pyrido[2,3-d]pyrimidine;

25 4-amino-5-(3-bromophenyl)-7-(4-(2-oxo-3-oxazolidinyl)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(2-propyl)-3-pyridinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(3-methyl-4-pyrrolidinylphenyl)pyrido[2,3-d]pyrimidine;

30 4-amino-5-(3-bromophenyl)-7-(6-imidazolyl-3-pyridinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-phenylmethyl-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(2-(3-aminopropynyl)phenylmethyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(1-(3-bromophenyl)ethyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(4-dimethylaminophenyl)-7-(4-bromophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(2-furanyl)-7-(4-(N-morpholinyl)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(2-dimethylamino-5-pyrimidinyl)pyrido[2,3-d]pyrimidine;

10 4-amino-5-(3-bromophenyl)-7-(4-(ureido)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(1-phenylmethyl-3-piperidinyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(3-methyl-5-isoxazolyl))-3-pyridinyl)pyrido[2,3-d]pyrimidine;

15 4-amino-5-(3-bromophenyl)-7-(6-chloro-3-pyridinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-methoxy-3-pyridinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(1,2,4-triazol-4-yl)-3-pyridinyl)pyrido[2,3-d]pyrimidine;

20 4-amino-5-(3-bromophenyl)-7-(2-morpholinyl-5-pyrimidinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(2-thiazolyl)-7-(4-pyrrolidinylphenyl)-pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-pyrazolyl-3-pyridinyl)-pyrido[2,3-d]pyrimidine;

25 4-amino-5-(3-bromophenyl)-7-(4-(1-methyl-ureido)phenyl)-pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(N-methyl-N-(2-pyrimidinyl)amino)phenyl)-pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(3-fluoro-4-(N-formyl-N-methylamino)phenyl)-

30 pyrido[2,3-d]pyrimidine;

4-formylamino-5-(3-bromophenyl)-7-(3-fluoro-4-(N-formyl-N-methylamino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(N-methyl-N-methylsulfonylamino)phenyl)pyrido[2,3-d]pyrimidine;

5 4-amino-5-(3-bromophenyl)-7-(6-(N-methyl-N-methylsulfonylamino)-3-pyridinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(1-methyl-5-indolinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(1-methyl-5-benzimidazolyl)pyrido[2,3-d]pyrimidine;

10 4-amino-5-(3-bromophenyl)-7-(6-dimethylamino-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3bromophenyl)-7-(6-morpholinyl-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-pyrrolidinyl-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

15 4-amino-5-(3-bromophenyl)-7-(5-morpholinyl-2-pyrazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(5-(N-(2-methoxyethyl)-N-methylamino)-2-pyrazinyl)pyrido[2,3-d]pyrimidine;

20 4-amino-5-(3-bromophenyl)-7-(4-(morpholinylmethyl)-phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(5-(N,N-bis(2-methoxyethyl)amino)-2-pyridinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(imidazolylmethyl)-phenyl)pyrido[2,3-d]pyrimidine;

25 4-amino-5-(3-bromophenyl)-7-(5-(1-morpholinyl)-2-pyridinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-((dimethylamino)methyl)-phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(5-(4-hydroxy-1-piperidinyl)-2-pyridinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(5-(N-formyl-N-methylamino)-2-pyridinyl)pyrido[2,3-d]pyrimidine;

5 4-amino-5-(3-bromophenyl)-7-(5-(2-propenyl)-2-pyridinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(3-(2-methoxyethyl)-2-oxo-6-benzoxazolyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(1-(N-formylamino)-ethyl)phenyl)pyrido[2,3-10 d]pyrimidine;

4-(methylamino)-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine hydrochloride;

4-(2-methoxyethylamino)-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine hydrochloride;

15 4-amino-5-(3-bromophenyl)-7-(4-(1-methyl-2-imidazolyl)phenyl)pyrido[2,3-d]pyrimidine trihydrochloride;

4-amino-5-(3-bromophenyl)-7-(4-(aminomethyl)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(2-bromo-4-(dimethylamino)phenyl)pyrido[2,3-d]pyrimidine;

20 4-amino-5-(3-bromophenyl)-7-(4-(dimethylaminoethyl)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(3-(dimethylamino)propynyl)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(3-amino-3-methylbutynyl)phenyl)pyrido[2,3-25 d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-dimethylphosphonatophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(3-(methoxypropynyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-carboxyphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-methyl-3-oxo-2H-4H-pyrido[3.2-b]-1,4-oxazin-7-yl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(2-dimethylamino)ethyl)-3-oxo-2H-4H-pyrido[3.2-b]-1,4-oxazin-7-yl)pyrido[2,3-d]pyrimidine;

5 4-amino-5-(3-bromophenyl)-7-(2,3-dihydro-3-(dimethylaminoethyl)-2-oxobenzoxazol-6-yl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-methyl-3-oxo-2H-4H-benzo-1,4-oxazin-7-yl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(2,2,4-trimethyl-3-oxo-2H-4H-benzo-1,4-oxazin-7-yl)pyrido[2,3-d]pyrimidine;

10 4-amino-5-cyclohexyl-7-(4-(2-dimethylamino)ethyl)-2H-4H-benzo-3-oxo-1,4-oxazin-7-yl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(5-(1-methylethyl)-2-pyridyl)pyrido[2,3-d]pyrimidine;

15 4-amino-5-(3-bromophenyl)-7-(5-piperidin-1-ylpyrid-2-yl)pyrido[2,3-d]pyrimidine;

4-amino-5-(1-(4-bromophenyl)ethyl)-7-(6-morpholinylpyrid-3-yl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-((N-formylamino)methyl)phenyl)pyrido[2,3-d]pyrimidine;

20 4-amino-5-(3-bromophenyl)-7-(4-(1-methyl-1-(N-methylamino)ethyl)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(1-dimethylamino)-1-methylethyl)phenyl)pyrido[2,3-d]pyrimidine;

25 4-amino-5-(3-bromophenyl)-7-(N-acetyl-5-indolinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(6-chloro-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(1-(2-bromophenyl)ethyl)-7-(6-diethylamino-3-pyridyl)pyrido[2,3-d]pyrimidine;

30 4-amino-5-(1-(2-bromophenyl)ethyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(1-(2-bromophenyl)ethyl)-7-(4-(N-methyl-N-formyl)amino)-phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(6-morpholiny1-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-((2-bromophenyl)methyl)-7-(6-morpholiny1-3-pyridyl)pyrido[2,3-d]pyrimidine;

5 4-amino-5-(4-tetrahydropyranyl)-7-(6-morpholiny1-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(6-dimethylamino-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(1-ethylpropyl)-7-(6-dimethylamino-3-pyridyl)pyrido[2,3-d]pyrimidine;

10 4-amino-5-cyclopentyl-7-(6-morpholiny1-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(2-chloro-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3,5-dimethylcyclohexyl)-7-(6-dimethylamino-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-((N-(benzyloxycarbonyl)-4-piperidinyl)methyl)-7-(6-morpholiny1-3-pyridyl)pyrido[2,3-d]pyrimidine;

15 4-amino-5-cyclohexyl-7-(6-bromo-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(3-cyanophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(1-(2-bromophenyl)ethyl)-7-(6-dimethylamino-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

20 4-amino-5-(3-bromophenyl)-7-(6-imidazolyl-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(azacycloheptanyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(N-methyl-N-(1-methylethyl))amino-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

25 4-amino-5-(1-(2-bromophenyl)ethyl)-7-(6-morpholiny1-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(6-(4-acetylpirerazinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(6-(4-acetyl-1,4-diazacycloheptanyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(6-(4-methyl-1,4-diazacycloheptanyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

5 4-amino-5-cyclohexyl-7-(6-(N-methyl-N-(2-(2-pyridyl)ethyl)amino)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(6-2-(N-(N',N'-dimethylaminoethyl)-N-methylamino)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(6-azetidinyl-3-pyridyl)pyrido[2,3-d]pyrimidine;

10 4-amino-5-cyclohexyl-7-(6-(3-(N-methylacetamido)pyrrolidinyl)pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(6-(3-(formamido)pyrrolidinyl)pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(4-oxo-1-phenyl-1,3,8-triazaspiro[4.5[decan-8-yl]pyrido[2,3-d]pyrimidine;

15 4-amino-5-cyclohexyl-7-(6-(2-methoxymethyl)pyrrolidin-1-yl)pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(6-(N-methoxyethyl-N-propylamino)pyridyl)pyrido[2,3-d]pyrimidine;

20 4-amino-5-cyclohexyl-7-(N-methyl-N-(2,2-dimethoxyethyl)amino)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(6-(4-(dimethylamino)piperidinyl)pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(6-(4-(aminocarbonyl))piperidinyl)pyridyl)pyrido[2,3-d]pyrimidine;

25 4-amino-5-cyclohexyl-7-(N-methyl-N-(3-(diethylamino)propyl)aminopyrid-3-yl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(6-(N-methyl-N-(4-pyridyl)ethylamino)pyrid-3-yl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(6-(N-methyl-N-(3-pyridylmethylamino)pyrid-3-yl)pyrido[2,3-d]pyrimidine;

4-amino-5-(1-(2-bromophenyl)ethyl)-7-(1-methyl-5-indolyl)pyrido[2,3-d]pyrimidine;

5 4-amino-5-(1-(2-bromophenyl)ethyl)-7-(1-methyl-2,3-dioxo-5-indolyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(3-fluoro-4-(1-morpholinyl)phenyl)pyrido[2,3-d]pyrimidine;

10 4-amino-5-(3-bromophenyl)-7-(4-hydroxy-3-nitrophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4,4-ethylenedioxy piperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-oxopiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

15 4-amino-5-(3-bromophenyl)-7-(6-(4-formylpiperazinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-methylpiperazinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-thiomorpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidin;

20 4-amino-5-(3-bromophenyl)-7-(6-(4,4-dioxothiomorpholinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(2-bromophenyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromo-4-methoxyphenyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine;

25 4-amino-5-(4-bromophenyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-chlorophenyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(5-chloro-6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine;

30 4-amino-5-(3-bromophenyl)-7-(6-(N-oxidomorpholinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(N-(2-hydroxyethoxyethyl)amino)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(N-(2-hydroxyethoxyethyl)-N-formylamino)-3-pyridyl)pyrido[2,3-d]pyrimidine;

5 4-amino-5-(3-bromophenyl)-7-(6-(N-(2-hydroxyethoxyethyl)-3-pyridyl-N-oxide)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(3-hydroxy)morpholinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

10 1-(5-(4-amino-5-(3-bromophenyl)pyrido[2,3-d]pyrimidin-7-yl)-2-pyridyl)-piperidine-4-phosphate, disodium salt;

4-amino-5-(3-bromophenyl)-7-(4-methylenylpiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-hydroxy-4-(hydroxymethyl)piperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

15 4-amino-5-(3-bromophenyl)-7-(6-(4,4-ethylenedioxypiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(6-(4-oxo-piperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(6-(4-methylenylpiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

20 4-N-(iminomethyl)amino-5-cyclohexyl-7-(6-dimethylamino-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-allylamino-5-(4-bromophenyl)-7-(4-dimethylaminophenyl) pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-hydroxypiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

25 4-amino-5-(cyclohexyl)-7-(6-(4,4-ethylenedioxypiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(2-morpholinyl-5-thiazolyl)pyrido[2,3-d]pyrimidine;

4-(N-(2,3-dihydroxypropyl)amino)-5-(3-bromophenyl)-7-(6-morpholinyl-3-pyridinyl)pyrido[2,3-d]pyrimidine;

4-(N-(3-morpholinylpropyl)amino)-5-(3-bromophenyl)-7-(6-morpholinyl-3-pyridinyl)pyrido[2,3-d]pyrimidine;

5 4-(N-(2-(4-imidazolyl)ethyl)amino)-5-(3-bromophenyl)-7-(6-morpholinyl-3-pyridinyl)pyrido[2,3-d]pyrimidine;

4-(N-(3-carboxypropyl)amino)-5-(3-bromophenyl)-7-(6-morpholinyl-3-pyridinyl)pyrido[2,3-d]pyrimidine;

(S)-4-amino-5-(3-bromophenyl)-7-(6-(O-methyl-2-hydroxymethylpyrrolidinyl)-3-10 pyridinyl)pyrido[2,3-d]pyrimidine;

(S)-4-amino-5-(3-bromophenyl)-7-(6-(2-hydroxymethylpyrrolidinyl)-3-pyridinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(2-bromophenyl)-7-(6-(4-hydroxypiperidinyl)-3-pyridinyl)pyrido[2,3-d]pyrimidine;

15 4-amino-5-(4-fluorophenyl)-7-(6-(4,4-ethylenedioxypiperidinyl)-3-pyridinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(2-bromophenyl)-7-(6-(4-hydroxypiperidinyl)-3-pyridazyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4,4-ethylenedioxypiperidinyl)-3-20 pyridazyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(2-morpholinyl-4-thiazolyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(N-methyl-3-indolyl)-7-(6-morpholinyl-3-pyridinyl)pyrido[2,3-d]pyrimidine;

25 4-amino-5-(3-bromophenyl)-7-(6-(4-ethoxyiminopiperidinyl)-3-pyridinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-ethoxycarbonylmethoxyiminopiperidinyl)-3-pyridinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-oxopiperidinyl)-3-pyridazinyl)pyrido[2,3-30 d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-morpholinyliminopiperidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptan-5-yl)-3-pyridazyl)pyrido[2,3-d]pyrimidine;

5 4-amino-5-(3-bromophenyl)-7-(6-(4-methoxyiminopiperidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-phenylmethoxy-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-methoxypiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

10 4-amino-5-(3-bromophenyl)-7-(6-(4-(4-tetrahydropyranloxy)iminopiperidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-isobutoxy-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-(N-methylpiperazinyl)iminopiperidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

15 4-amino-5-(3-bromophenyl)-7-(6-(4-tetrahydropyranloxy)-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-morpholinylethoxy-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-ethoxypiperidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

20 4-amino-5-(3-bromophenyl)-7-(6-(4-(2-ethoxyethoxy)piperidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-(4-tetrahydropyranloxyethyl)piperidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

25 4-amino-5-(3-bromophenyl)-7-(6-(3-(R)-tetrahydrofuranloxy)piperidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(3-(S)-tetrahydrofuranloxy)piperidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(trans-3-ethoxy-4-hydroxy)pyrrolidinyl)-3-

30 pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(*cis*-3-ethoxy-4-hydroxy)pyrrolidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(*trans*-3-ethoxy-4-hydroxy)pyrrolidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

5 4-amino-5-(3-bromophenyl)-7-(6-(*trans*-3,4-bis-ethoxy)pyrrolidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(*trans*-3,4-bis-ethoxy)pyrrolidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

10 4-amino-5-(3-bromophenyl)-7-(6-(*cis*-3,4-bis-ethoxy)pyrrolidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(*cis*-3,4-bis-ethoxy)pyrrolidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(*cis*-3-ethoxy-4-hydroxy)pyrrolidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

15 4-amino-5-(3-bromophenyl)-7-(6-(*cis*-3-amino-4-hydroxy)pyrrolidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(*cis*-3-amino-4-hydroxy)pyrrolidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(2-pyridyl)-7-(6-(1,4-dioxa-8-azaspiro[4.5]decan-8-yl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

20 4-amino-5-(2,3-dichlorophenyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(2-pyridyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(2-ethoxyphenyl)-7-(6-(1,4-dioxa-8-azaspiro[4.5]decan-8-yl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

25 4-amino-5-(2-bromo-5-ethoxyphenyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(2,5-dichlorophenyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(2,5-dimethylphenyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine

4-amino-5-(3-fluorophenyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-trifluoromethylphenyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-fluoro-5-trifluoromethylphenyl)-7-(6-(1,4-dioxa-8-azaspiro[4.5]decan-8-yl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

5 4-amino-5-(3,5-diclorophenyl)-7-(6-(1,4-dioxa-8-azaspiro[4.5]decan-8-yl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(1,5-dioxa-9-azaspiro[5.5]undecan-9-yl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(4-bromo-2-thienyl)-7-(6-(1,4-dioxa-8-azaspiro[4.5]decan-8-yl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

10 4-amino-5-(3-bromophenyl)-7-(6-(4-tertbutyl)piperidinyl-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-N-formyl)piperidinyl-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

15 4-amino-5-(3-bromo-2-thienyl)-7-(6-(4,4-ethylenedioxypiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-cyanophenyl)-7-(6-morpholinyl-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-Bromophenyl)-7-(6-(S-O-ethyl-2-hydroxymethylpyrrolidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

20 4-amino-5-(3-bromophenyl)-7-(6-(4,4-(cis-1,2-dioxycyclopentyl)piperidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-((2S,3S)-2,3-dimethyl-1,4-dioxa-8-azaspiro[4.5]decan-8-yl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4,4-(cis-1,2-dioxycyclopentyl)piperidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

25 4-amino-5-(3-bromophenyl)-7-(6-(4-acetyl-1-oxa-4,8-diazaspiro[4.5]decan-8-yl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-((2R,3R)-2,3-bis(methoxymethyl)-1,4-dioxa-8-azaspiro[4.5]decan-8-yl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4,4-(cis-3,4-dioxy-oxacyclopentyl)piperidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

30 4-amino-5-(3-bromophenyl)-7-(6-(4,4-(cis-3,4-dioxy-oxacyclopentyl)piperidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(3-methoxy-1,5-dioxa-9-azaspiro[5.5]undecan-9-yl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(1,5-dioxa-3-hydroxymethyl-9-azaspiro[5.5]undecan-9-yl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

5 4-amino-5-(3-bromophenyl)-7-(6-(1,7,14-trioxa-11-azadispiro[4.2.5.2]pentadecan-11-yl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(4-tetrahydropyranyl)-7-(6-morpholinyl-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-morpholinyliminopiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

10 4-amino-5-(3-bromophenyl)-7-(6-(4-(N-methylpiperazinyl)iminopiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-(1,2,4-triazol-1-yl)iminopiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

15 4-amino-5-(3-indolyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(5-indolyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-ethylpiperidinylcarboxylate)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(2-phenylmethyl-3(2H)-pyridazinone-6-yl)pyrido[2,3-d]pyrimidine;

20 4-amino-5-(3-bromophenyl)-7-(6-(4-(morpholinylcarboxamide)piperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-(N-morpholinylaminocarboxamide)piperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-(N,N-dimethylaminocarboxamide)piperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

25 4-amino-5-(3-bromophenyl)-7-(6-(4-(N-methyl-N-methoxyethylcarboxamide)piperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(4-quinolyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-(N-methoxyethylcarboxamide)piperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-hydroxymethylpiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

5 4-amino-5-(2-bromophenyl)-7-(6-(1,4-dioxa-8-azaspiro[4.5]decan-8-yl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(2-bromophenyl)-7-(6-(4-hydroxypiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-N-acetylpirazinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

10 4-amino-5-(3-bromophenyl)-7-(6-(4-cyanopiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-N-(4-fluorophenyl)piperazinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(4-fluorophenyl)-7-(6-morpholiny-3-pyridyl)pyrido[2,3-d]pyrimidine;

15 4-amino-5-(3-bromophenyl)-7-(4-morpholinybenzenesulfonamide)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-N-1,4-dioxa-8-azaspiro[4.5]decan-8-ylbenzenesulfonamide)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-N-cyclopropylbenzenesulfonamide)pyrido[2,3-d]pyrimidine;

20 4-amino-5-(3-bromophenyl)-7-(4-piperidinebenzenesulfonamide)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(4-cyanopiperidine)benzenesulfonamide)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-N-cyclopropylmethylbenzenesulfonamide)pyrido[2,3-d]pyrimidine;

25 4-amino-5-(3-bromophenyl)-7-(4-N,N-dimethylaminobenzenesulfonamide)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-N-(S)-2-hydroxymethylpyrrolidinebenzenesulfonamide)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(4-hydroxypiperidine)benzenesulfonamide)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(cis-3,5-dimethylmorpholinyl)benzenesulfonamide)pyrido[2,3-d]pyrimidine;

5 4-amino-5-(3-bromophenyl)-7-(3-fluoro-4-thiomorpholinylphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(4-fluorophenyl)-7-(6-(thiomorpholinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(4-fluorophenyl)-7-(6-(4,4-dioxothiomorpholinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

10 4-methoxy-5-(3-bromophenyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(4-dioxa-8-azaspiro[4.5]decan-8-ylcarboxamide)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(N-cyclopropylcarboxamide)phenyl)pyrido[2,3-d]pyrimidine;

15 4-amino-5-(3-bromophenyl)-7-(4-(morpholinylcarboxamide)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-N-cyclopropylamino-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(4-hydroxypiperidinylcarboxamide)phenyl)pyrido[2,3-d]pyrimidine;

20 4-amino-5-(3-bromophenyl)-7-(6-(S)-hydroxymethylpyrrolidinyl-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-(2-ethoxyethoxy)piperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-hexahydropyrimidine-3-pyridyl)pyrido[2,3-d]pyrimidine;

25 4-amino-5-(4,4-difluorocyclohexyl)-7-(6-(1,4-dioxa-8-azaspiro[4.5]decan-8-yl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(S)-2-ethoxyethoxypyrrrolidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(R)-2-ethoxyethoxypyrrolidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(cis-3,4-dihydroxypyrrolidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

5 4-amino-5-(3-bromophenyl)-7-((3aR,6aS)-2-oxo-tetrahydro-3aH-[1,3]dioxolo[4,5-c]pyrrol-5-yl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(cis-2,3-dihydroxypyrrolidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(S,R-2-hydroxymethyl-4-hydroxypyrrolidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

10 4-amino-5-(3-bromophenyl)-7-(6-(R-2-hydroxymethyl-4-pyrrolidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptan-5-yl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

15 4-amino-5-(3-bromophenyl)-7-(6-(2-imidizolidone-1-yl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(1,1-dimethyl-3-butenyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(2,4-dioxo-(1H,3H)-quinazolin-3-yl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

20 4-amino-5-(3-bromophenyl)-7-(6-carboxamide-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-morpholinylcarboxamide-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-methoxy-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-N,N-diethoxyethylamino-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

25 4-amino-5-(3-bromophenyl)-7-(6-(4-ethoxymethylpiperidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-(4-tetrahydropyranoyloxymethyl)piperidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-ethoxyethoxymethyl)piperidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-N-methyl-N-1,3-dioxalanemethylamino)-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

5 4-amino-5-(3-bromophenyl)-7-(6-(1,4-dioxaspiro[4.5]decanyl-8-oxy)-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-dihydroxymethylmethoxy-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

10 4-amino-5-(3-bromophenyl)-7-(6-(3-pyridyloxy)-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4,7-epoxy-7-methyl-2,3,3A,4,5,6,7,7a-octahydro-1H-isoindolyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-N-ethyl-N-methoxyethyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

15 4-amino-5-(3-bromophenyl)-7-(6-(4-N-methyl-N-methoxyethyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(3,4-dimethoxymethoxypyrrolidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(hexahydro-1H-furo[3,4-c]pyrrol-5-yl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

20 4-amino-5-(3-bromophenyl)-7-(6-(hexahydro-1H-furo[3,4-c]pyrrol-5-yl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(trans-3-hydroxy-4-methylpyrrolidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(trans-3-hydroxy-4-methylpyrrolidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

25 4-amino-5-(3-bromophenyl)-7-(6-(cis-3-hydroxy-4-methylpyrrolidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(cis-3-hydroxy-4-methylpyrrolidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(trans-3-cyano-4-hydroxylpyrrolidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(3-hydroxy-4-tert-butylcarboxamide)pyrrolidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

5 4-amino-5-(3-bromophenyl)-7-(6-(S-2-(4-tetrahydropyranloxy)methyl)pyrrolidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(3-(4-tetrahydropyranloxy)iminopyrrolidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(2-morpholinyl-5-thiazoyl)pyrido[2,3-d]pyrimidine;

10 4-amino-5-(3-bromophenyl)-7-(5-bromo-2-thienyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(2,5-dimethyl-3-thienyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(5-chloro-2-thienyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(2,4-dimethyl-5-thiazoyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(5-methyl-2-thienyl)pyrido[2,3-d]pyrimidine;

15 4-amino-5-(3-bromophenyl)-7-(2-furanyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(2-(1,4-dioxa-8-azaspiro[4.5]decan-8-yl)-5-thiazoyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(3-thienyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(3-methyl-2-thienyl)pyrido[2,3-d]pyrimidine;

20 4-amino-5-(3-bromophenyl)-7-(2-morpholinyl-4-thiazoyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(2-morpholinyl-4-trifluoromethyl-5-thiazoyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(5-morpholinyl-2-thienyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-methyl-2-morpholinyl-5-thiazoyl)pyrido[2,3-d]pyrimidine;

25 4-amino-5-(3-bromophenyl)-7-(2,5-dichloro-3-thienyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(2,5-dimethyl-3-furanyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(N-methyl-2-pyrrolyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(2-N,N-dimethylamino-5-thiazoyl)pyrido[2,3-d]pyrimidine;

30 4-amino-5-(3-bromophenyl)-7-(2-N,N-dimethylamino-5-thiazoyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(2-morpholinyl-5-thiazoyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(2-(4,4-dioxythiomorpholinyl)-5-thiazoyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(2-(1,1-dioxidothiomorpholinyl)-5-thiazoyl)pyrido[2,3-d]pyrimidine;

5 4-amino-5-(3-bromophenyl)-7-(2-N-methyl-N-methoxyethylamino-5-thiazoyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(2-N-methyl-N-ethylamino-5-thiazoyl)pyrido[2,3-d]pyrimidine;

10 4-amino-5-(3-bromophenyl)-7-(2-N-pyrrolidinyl-5-thiazoyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(2-N-methyl-N-propylamino-5-thiazoyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(2-N,N-diethylamino-5-thiazoyl)pyrido[2,3-d]pyrimidine;

15 4-amino-5-(3-bromophenyl)-7-(2-(N-methylpiperazinyl)-5-thiazoyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(2-(N-(2-pyridyl)piperazinyl)-5-thiazoyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(2-N-methy-N-(2-pyridylethyl)-5-thiazoyl)pyrido[2,3-d]pyrimidine;

20 4-amino-5-(3-bromophenyl)-7-(2-(4-oxopiperazinyl)-5-thiazoyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(2-(4-(N-morpholinyl)iminopiperazinyl)-5-thiazoyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-N-morpholine-3-pyridinesulfonamide)pyrido[2,3-d]pyrimidine;

25 4-amino-5-(3-bromophenyl)-7-(2-(4-oxopiperidinyl)-5-pyrimidyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(2-(4,4-dioxethylenepiperidinyl)-5-pyrimidyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(5-(1,4-dioxa-8-azaspiro[4.5]decan-8-yl)-2-pyrazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(5-(4-oxopiperidinyl)-2-pyrazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-N-cyclopropyl-3-pyridinesulfonamide)pyrido[2,3-d]pyrimidine;

5 4-amino-5-(3-bromophenyl)-7-(6-(N-1,4-dioxa-8-azaspiro[4.5]decan-8-yl)-3-pyridylsulfonamide)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(2-(4-(4-tetrahydropyranloxy)iminopiperidinyl)-5-pyrazinyl)pyrido[2,3-d]pyrimidine;

10 4-amino-5-(3-bromophenyl)-7-(6-(4-(phenylmethoxy)iminopiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-(tert-butyloxy)iminopiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-(cyclohexyloxy)iminopiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

15 4-amino-5-(3-bromophenyl)-7-(6-(4-hydroxyiminopiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-tetrahydropyranloxy)iminopiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

20 4-amino-5-(3-bromophenyl)-7-(6-(4-methoxyethoxyiminopiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-(2-phenylmethoxy)iminopiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-(5¹H-2-oxyfuranyl)-4-hydroxypiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

25 4-amino-5-(3-bromophenyl)-7-(6-(4-(1-(4-tetrahydropyranloxy)iminoethyl)-4-hydroxypiperidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-(4'-acetyl-4'-hydroxypiperidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-(1-(isopropylcarboxymethoxy)iminoethyl))-4-hydroxypiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-(1-(ethylcarboxymethoxy)iminoethyl))-4-hydroxypiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

5 4-amino-5-(3-bromophenyl)-7-(6-(4-(1-(methylcarboxymethoxy)iminoethyl))-4-hydroxypiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-(1-(2-tetrahydropyranloxy)iminoethyl))-4-hydroxypiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-(1-(allyloxy)iminoethyl))-4-hydroxypiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

10 4-amino-5-(3-bromophenyl)-7-(6-(4-(1-(ethoxy)iminoethyl))-4-hydroxypiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-(1-(methoxy)iminoethyl))-4-hydroxypiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-(1-(hydroxy)iminoethyl))-4-hydroxypiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

15 4-amino-5-(3-bromophenyl)-7-(6-(4-(1-(4-hydroxy-4-(4-tetrahydropyranloxy)iminoethyl))-4-hydroxypiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-(isopropylcarboxymethoxy)iminopiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-(3-butyrolactone)-4-hydroxypiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

20 4-amino-5-(3-bromophenyl)-7-(6-(4-(2-butyrolactone)-4-hydroxypiperidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-acetyl-4-hydroxypiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(3-hydroxyazetidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

25 4-amino-5-(3-bromophenyl)-7-(6-(4-(1-(4-tetrahydropyranloxy)iminoethyl))-4-hydroxypiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(3-hydroxyazetidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

30 4-amino-5-(3-bromophenyl)-7-(6-(3-hydroxyazetidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-((1*R*,5*S*)-3-hydroxy-8-azabicyclo[3.2.1]octan-8-yl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(*cis*-2,3-dihydroxypiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

5 4-amino-5-(3-bromophenyl)-7-(6-(*N*-methyl-*N*-(3-pyridylmethyl)amino)-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(1,2,3,6-tetrahydropyridyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-(*N*-4'methoxyphenylcarbamoyl)piperidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

10 4-amino-5-(3-bromophenyl)-7-(6-(4-(2-butyrolactone)-4-hydroxypiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(*trans*-3,4-bis(*N*-4'methoxyphenylcarbamoyl)pyrrolidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

15 4-amino-5-(3-bromophenyl)-7-(6-((1*S*,5*R*)-3-hydroxy-8-azabicyclo[3.2.1]octan-8-yl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(*S,S*-*trans*-3,4-dihydroxypyrrolidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(*R,R*-*trans*-3,4-dihydroxypyrrolidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

20 4-amino-5-(3-bromophenyl)-7-(6-(*R,R*-*trans*-3,4-dihydroxypyrrolidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-oxo-1-phenyl-1,3,8-triazaspiro[4.5]decan-8-yl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(1-oxa-4-oxo-4-thia-8-azaspiro[4.5]decan-8-yl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

25 4-amino-5-(3-bromophenyl)-7-(6-(1-oxa-4,4-dioxido-4-thia-8-azaspiro[4.5]decan-8-yl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-oxo-1-phenyl-1,3,8-triazaspiro[4.5]dec-2-en-8-yl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

30 4-amino-5-(3-bromophenyl)-7-(6-(4-oxo-1-phenyl-1,3,8-triazaspiro[4.5]dec-2-en-8-yl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-(2-keto-1-benzimidazoliny)l)piperidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-oxothiomorpholiny)l)-3-pyridyl)pyrido[2,3-d]pyrimidine;

5 4-amino-5-(3-bromophenyl)-7-(6-(4-(2-keto-1-benzimidazoliny)l)piperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(N-methyl-N-(2-pyridylethyl)amino)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(N-methyl-N-(4-pyridylethyl)amino)-3-pyridyl)pyrido[2,3-d]pyrimidine;

10 4-amino-5-(3-bromophenyl)-7-(6-(2-hydroxymethylpiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-N-(3-pyridylmethyl)amino-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(2-hydroxymethylpiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

15 4-amino-5-(3-bromophenyl)-7-(6-(1-oxa-4-thia-8-azaspiro[4.5]decan-8-yl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-hydroxy-4-(4-bromophenyl)piperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-N-(2-pyridinyl)piperazinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

20 4-amino-5-(3-bromophenyl)-7-(6-(4-N-(2-hydroxyethoxyethyl)piperazinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4,4-diacetoxyethylthio)piperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(N-methy-N-(3-pyridylmethyl)amino)-3-pyridyl)pyrido[2,3-d]pyrimidine;

25 4-amino-5-(3-bromophenyl)-7-(6-(4-pyrrolidinylpiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(2-(1H-imidazol-4-yl)ethylamino)-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

30 4-amino-5-(3-bromophenyl)-7-(6-(2-(1H-imidazol-4-yl)ethylamino)-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-N-cyanomethylpiperazinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(3-hydroxypyrroldinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

5 4-amino-5-(3-bromophenyl)-7-(6-(4-methylpiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(cis-3,5-dimethylmorpholinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4,4-difluoropipridinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

10 4-amino-5-(3-bromophenyl)-7-(6-(1,1-dioxidoythiomorpholinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-thiazolidinyl-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(1,1-dioxidoythiazolidin-3-yl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

15 4-amino-5-(3-bromophenyl)-7-(6-thiomorpholinyl-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(2,5-dihydropyrrolyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

20 4-amino-5-(3-bromophenyl)-7-(6-(1,3-dioxa-8-azaspiro[4.5]decan-8-yl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-hydroxy-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

amino-5-(2,3-dichlorophenyl)-7-(6-(1,4-dioxa-8-azaspiro[4.5]decan-8-yl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

25 4-amino-5-isopropyl-7-(6-(1,4-dioxa-8-azaspiro[4.5]decan-8-yl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-piperidinyl-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(3-(4-tetrahydropyranoyloxyimino)pyrrolidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine; and

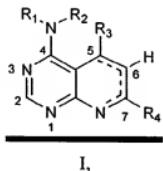
4-amino-5-(2-trifluorophenylphenyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine.

7. A pharmaceutical composition comprising a therapeutically effective amount of a 5 compound according to Claim 1 in combination with a pharmaceutically acceptable carrier.

8. A method of treating ischemia, neurological disorders, nociception, 10 inflammation, immunosuppression, gastrointestinal dysfunctions, diabetes and sepsis in a mammal in need of such treatment, comprising administering to the mammal a therapeutically effective amount of a compound according to Claim 1 or 3.

9. A method according to Claim 8 wherein the method consists of treating cerebral ischemia, myocardial ischemia, angina, coronary artery bypass graft surgery, percutaneous 15 transluminal angioplasty, stroke, thrombotic and embolic conditions, epilepsy, anxiety, schizophrenia, pain perception, neuropathic pain, visceral pain, arthritis, sepsis, diabetes and abnormal gastrointestinal motility.

10. A compound of formula I



or a pharmaceutically acceptable salt or amide thereof wherein,

R¹ and R² are each independently selected from the group consisting of hydrogen, 25 alkenyl, alkoxyalkyl, alkoxyalkylcarbonyl, alkoxy carbonyl, alkoxy carbonylalkyl, alkyl, alkylcarbonyl, aminocarbonyl, aryl, arylalkyl, arylalkylcarbonyl, arylcarbonyl, carboxyalkyl, formyl, haloalkylcarbonyl, heterocycle, heterocyclealkyl, heterocyclecarbonyl, hydroxyalkyl, iminoalkyl, and (NZ₂Z₃)alkyl, or R¹ and R² may join

together with the nitrogen atom to which they are attached to form a 5-7 membered ring optionally containing 1-2 additional heteroatoms selected from the group consisting of O, N, and S;

5 Z_1 and Z_2 are each independently selected from the group consisting of hydrogen, alkoxy carbonyl, alkyl, alkyl carbonyl, benzyl, benzyloxy carbonyl, and formyl;

R^3 is selected from the group consisting of alkenyl, alkyl, alkynyl, aryl, arylalkyl, cycloalkyl, cycloalkylalkyl, heterocycle, heterocyclealkyl, heterocyclealkylcarbonyl, $(NZ_1Z_2)alkyl$, and $-R^A R^B$;

10 R^A is selected from the group consisting of aryl and arylalkyl;
 R^B is selected from aryl, arylalkoxy, arylalkyl, aryloxy, heterocycle, and heterocyclealkyl;

R^4 is selected from the group consisting of alkenyl, alkoxy alkynyl, alkyl, alkynyl, cycloalkyl, aryl, arylalkyl, heterocycle, heterocyclealkyl, and $-R^C R^D R^E$;

15 R^C is selected from aryl, arylalkyl, heterocycle, and heterocyclealkyl;
 R^D is selected from aryl, arylalkoxy, arylalkoxyimino, arylalkyl, aryloxy, heterocycle, heterocyclealkoxy, heterocyclealkyl, heterocyclecarbonyl, heterocycleimino, heterocycleoxy, heterocycleoxyalkyl, heterocycleoxyimino, heterocycleoxyiminoalkyl, and heterocyclesulfonyl;

20 R^E is absent or selected from aryl, arylalkoxy, arylalkoxyimino, arylalkyl, aryloxy, heterocycle, heterocyclealkoxy, heterocyclealkyl, heterocyclecarbonyl, heterocycleimino, heterocycleoxy, heterocycleoxyalkyl, heterocycleoxyimino, heterocycleoxyiminoalkyl, and heterocyclesulfonyl; and

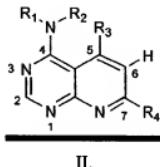
a dashed line --- indicates that a double bond is optionally present provided that proper valencies are maintained;

25 with the proviso that the following compounds are excluded,
4-amino-5-(4-chlorophenyl)-7-(4-nitrophenyl)pyridol[2,3-d]pyrimidine,
4-amino-5-(4-methoxyphenyl)-7-(4-nitrophenyl)pyridol[2,3-d]pyrimidine,
4-amino-5-(4-fluorophenyl)-7-(4-fluorophenyl)pyridol[2,3-d]pyrimidine,
4-amino-5-(4-chlorophenyl)-7-(4-fluorophenyl)pyridol[2,3-d]pyrimidine,
30 4-amino-5-phenyl-7-(4-aminophenyl)pyrido[2,3-d]pyrimidine,

4-amino-5-phenyl-7-(4-bromophenyl)pyrido[2,3-d]pyrimidine,
 4-amino-5-(4-methoxyphenyl)-7-(4-aminophenyl)pyrido[2,3-d]pyrimidine,
 4-amino-5-(4-methoxyphenyl)-7-(4-bromophenyl)pyrido[2,3-d]pyrimidine, and
 4-amino-5,7-diphenylpyrido[2,3-d]pyrimidine.

5

11. A compound according to claim 10 of formula II



or a pharmaceutically acceptable salt or amide thereof wherein,

10 R^1 and R^2 are independently selected from the group consisting of hydrogen, alkenyl, alkoxyalkyl, alkoxyalkylcarbonyl, alkoxycarbonyl, alkyl, alkylcarbonyl, aminocarbonyl, aryl, arylcarbonyl, carboxyalkyl, formyl, haloalkylcarbonyl, heterocyclealkyl, hydroxyalkyl, iminoalkyl, and $(NZ_1Z_2)alkyl$, or R^1 and R^2 may join together with the nitrogen atom to which they are attached to form a 6 membered ring
 15 optionally containing 1 additional heteroatom selected from the group consisting of O, N, and S;
 Z_1 and Z_2 are each independently selected from the group consisting of hydrogen, alkoxycarbonyl, alkyl, alkylcarbonyl, benzyl, benzyloxycarbonyl, and formyl;
 R^3 is selected from the group consisting of alkenyl, alkyl, aryl, arylalkyl,
 20 cycloalkyl, heterocycle, heterocyclealkyl, $(NZ_1Z_2)alkyl$, and $-R^A R^B$;
 R^A is selected from the group consisting of aryl and arylalkyl;
 R^B is selected from the group consisting of aryl, arylalkoxy, arylalkyl, aryloxy, and heterocycle;
 R^4 is selected from the group consisting of alkoxyalkynyl, alkynyl, aryl,
 25 heterocycle, and $-R^C R^D R^E$;
 R^C is selected from the group consisting of aryl and heterocycle;

R^D is selected from the group consisting of aryl, arylalkoxy, arylalkyl, aryloxy, heterocycle, heterocyclealkoxy, heterocyclealkyl, heterocyclecarbonyl, heterocycleoxy, and heterocyclesulfonyl; and

R^E is absent or selected from the group consisting of aryl, arylalkoxy, 5 arylalkoxyimino, arylalkyl, aryloxy, heterocycle, heterocyclealkoxy, heterocyclealkyl, heterocyclecarbonyl, heterocycleimino, heterocycleoxy, heterocycleoxyalkyl, heterocycleoxyimino, and heterocycleoxyiminoalkyl.

12. A compound according to claim 10 wherein R^4 is selected from the group 10 consisting of:

phenyl; thiophene-2-yl; 3-methyl-2-oxobenzoxazolin-6-yl; 2-(dimethylamino)-5-pyrimidinyl; 2-(N-formyl-N-methyl amino)-5-pyrimidinyl; 2-(N-methoxyethyl-N-methyl amino)-5-pyrimidinyl; 2-(N-methylamino)-5-pyrimidinyl; 2-(1-morpholinyl)-5-pyrimidinyl; 2-(1-pyrrolidinyl)-5-pyrimidinyl; 2-dimethylamino-5-pyrimidinyl; 2-furanyl; 15 2-oxobenzoxazolin-6-yl; 2-pyridyl; 3-(dimethylamino)phenyl; 3-amino-4-methoxyphenyl; 3-bromo-4-(dimethylamino)phenyl; 3-methoxyphenyl; 3-methyl-4-(N-acetyl-N-methylamino)phenyl; 3-methyl-4-(N-formyl-N-methylamino)phenyl; 3-methyl-4-(N-methyl-N-(trifluoroacetyl)amino)phenyl; 3-methyl-4-(N-methylamino)phenyl; 3-methyl-4-pyrrolidinylphenyl; 3-pyridyl; 3,4-dichlorophenyl; 3,4-methylenedioxophenyl; 3,4,5-trimethoxyphenyl; 4-(acetylamino)phenyl; 4-(dimethylamino)-3-fluorophenyl; 4-(dimethylamino)phenyl; 4-(imidazol-1-yl)phenyl; 4-(methylthio)phenyl; 4-(morpholinyl)phenyl; 4-(N-(2-(dimethylamino)ethyl)amino)phenyl; 4-(N-(2-methoxyethyl)amino)phenyl; 4-(N-acetyl-N-methylamino)phenyl; 4-(N-ethyl-N-formylamino)phenyl; 4-(N-ethylamino)phenyl; 4-(N-formyl-N-(2-methoxyethyl)amino)phenyl; 4-(N-isopropylamino)phenyl; 4-(N-methyl-N-(2-dimethylamino)ethyl)amino)phenyl; 4-(N-methyl-N-(2-phthalimidyl)acetyl)amino)phenyl; 4-(N-methyl-N-(2-cyano)ethylamino)phenyl; 4-(N-methyl-N-(2-methoxyethyl)amino)phenyl; 4-(N-methyl-N-(3-methoxy)propionylamino)phenyl; 4-(N-methyl-N-acetyl)amino)phenyl; 4-(N-methyl-N-formylamino)phenyl; 4-(N-methyl-N-trifluoroacetyl)amino)phenyl; 4-(N-

morpholinyl)phenyl; 4-(thiophene-2-yl)phenyl; 4-(ureido)phenyl; 4-(2-(dimethylamino)acetyl amino)phenyl; 4-(2-methoxy)acetyl amino)ethyl)amino)phenyl; 4-(2-methoxyethoxyphenyl; 4-(2-oxo-3-oxazolidinyl)phenyl; 4-(4-methoxy-2-butyl)phenyl; 4-(4-methylpiperidinyl)phenyl; 4-(5-pyrimidinyl)phenyl; 4-aminophenyl; 4-bromophenyl;

5 4-butoxyphenyl; 4-carboxamidophenyl; 4-chlorophenyl; 4-cyanophenyl; 4-diethylaminophenyl; 4-diethylmalonylallylphenyl; 4-dimethylaminophenyl; 4-ethoxyphenyl; 4-ethylphenyl; 4-fluorophenyl; 4-hydroxyphenyl; 4-imidazolylphenyl; 4-iodophenyl; 4-isopropylphenyl; 4-methoxyphenyl; 4-methylaminophenyl; 4-methylsulfonylphenyl; 4-morpholinylphenyl; 4-N-(2-(dimethylamino)ethyl)-N-

10 formylamino)phenyl; 4-N-(3-methoxypropionyl)-N-isopropyl-amino)phenyl; 4-N-ethyl-N-(2-methoxyethyl)amino)phenyl; 4-N-formylpiperazinylphenyl) 4-nitrophenyl; 4-piperidinylphenyl; 4-(3-pyridyl)phenyl; 4-pyrrolidinylphenyl; 4-t-butylacrylphenyl; 5-(dimethylamino)thiophene-2-yl; 5-amino-2-pyridyl; 5-dimethylamino-2-pyrazinyl; 3-dimethylaminopyridazin-6-yl; 5-dimethylamino-2-pyridyl; 5-pyrimidinylphenyl; 6-(N-

15 methyl-N-formylamino)-3-pyridinyl; 6-(N-methyl-N-methoxyethylamino)-3-pyridinyl; 6-(2-oxo-3-oxazolidinyl)-3-pyridinyl; 6-dimethylamino-3-pyridinyl; 6-imidazolyl-3-pyridinyl; 6-morpholinyl-3-pyridinyl; 6-pyrrolidinyl-3-pyridinyl; 6-(2-propyl)-3-pyridinyl; (4-formylamino)phenyl; 6-(4-oxopiperidinyl)-3-pyridazinyl; 6-(4-

20 morpholinyliminopiperidinyl)-3-pyridazinyl; 6-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptan-5-yl)-3-pyridazinyl; 6-(4-methoxyiminopiperidinyl)-3-pyridazinyl; 6-phenylmethoxy-3-pyridazinyl; 6-(1,1-dioxidothiazolidin-3-yl)-3-pyridyl; 6-(1,3-dioxa-8-azaspiro[4.5]decan-8-yl)-3-pyridyl; 6-(1,1-dioxidothiomorpholinyl)-3-pyridazinyl; 6-(1-oxa-4,4-dioxido-4-thia-8-azaspiro[4.5]decan-8-yl)-3-pyridyl; 6-(1-oxa-4-oxo-4-thia-8-azaspiro[4.5]decan-8-yl)-3-

25 pyridyl; 6-(3-hydroxy-8-azabicyclo[3.2.1]octan-8-yl)-3-pyridyl; 6-(4-oxo-1-phenyl-1,3,8-triazaspiro[4.5]decan-8-yl)-3-pyridyl; 6-(4-oxo-1-phenyl-1,3,8-triazaspiro[4.5]dec-2-en-8-yl)-3-pyridyl; 6-(N-1,4-dioxa-8-azaspiro[4.5]decan-8-yl)-3-pyridylsulfonamide; 2-(1,1-dioxidothiomorpholinyl)-5-thiazoyl; 5-(1,4-dioxa-8-azaspiro[4.5]decan-8-yl)-2-pyrazinyl; 2-(1,4-dioxa-8-azaspiro[4.5]decan-8-yl)-5-thiazoyl; 6-(hexahydro-1H-furo[3,4-c]pyrrol-5-

30 yl)-3-pyridazinyl; 6-(hexahydro-1H-furo[3,4-c]pyrrol-5-yl)-3-pyridyl; 6-(4-

methoxypiperidinyl)-3-pyridyl; 6-(4,7-epoxy-7-methyl-2,3,3A,4,5,6,7,7a-octahydro-1H-isoindolyl)-3-pyridazinyl; 6-(4-(4-tetrahydropyranoyloxy)iminopiperidinyl)-3-pyridazinyl; 6-isopropoxy-3-pyridazinyl; 6-(2,4-dioxa-(1H,3H)-quinazolin-3-yl)-3-pyridyl; 6-(4-(N-methylpiperazinyl)iminopiperidinyl)-3-pyridazinyl; 6-(4-tetrahydropyranoyloxy)-3-
5 pyridazinyl; 6-morpholinylethoxy-3-pyridazinyl; 6-(4-ethoxypiperidinyl)-3-pyridazinyl; 6-(1,4-dioxa-8-azaspiro[4.5]decan-8-yl)-3-pyridyl; 6-(4-(2-ethoxyethoxy)piperidinyl)-3-pyridazinyl; 6-((3aR,6aS)-2-oxo-tetrahydro-3aH-[1,3]dioxolol[4,5-c]pyrrol-5-yl)-3-pyridyl; 6-(4-(4-tetrahydropyranoyloxyethyl)piperidinyl)-3-pyridazinyl; 6-(3-(R)-tetrahydrofuranyl-oxo)piperidinyl)-3-pyridazinyl; 6-(3-(S)-tetrahydrofuranyl-oxo)piperidinyl)-3-pyridazinyl; 6-(trans-3-ethoxy-4-
10 hydroxy)pyrrolidinyl)-3-pyridazinyl; 6-(cis-3-ethoxy-4-hydroxy)pyrrolidinyl)-3-pyridazinyl; 6-(trans-3-ethoxy-4-hydroxy)pyrrolidinyl)-3-pyridyl; 6-(trans-3,4-bis-ethoxy)pyrrolidinyl)-3-pyridazinyl; 6-(trans-3,4-bis-ethoxy)pyrrolidinyl)-3-pyridyl; 6-(cis-3,4-bis-ethoxy)pyrrolidinyl)-3-pyridazinyl;
15 6-(cis-3-ethoxy-4-hydroxy)pyrrolidinyl)-3-pyridyl; 6-(cis-3-amino-4-hydroxy)pyrrolidinyl)-3-pyridazinyl; 6-(cis-3-amino-4-hydroxy)pyrrolidinyl)-3-pyridyl; 6-(1,5-dioxa-9-azaspiro[5.5]undecan-9-yl)-3-pyridazinyl; 6-(4-tertbutyl)piperidinyl-3-pyridazinyl; 6-(4-N-formyl)piperidinyl-3-pyridazinyl; 6-morpholinyl-3-pyridazinyl; 4-N-1,4-dioxa-8-azaspiro[4.5]decan-8-ylbenzenesulfonamide; 4-(4-dioxa-8-
20 azaspiro[4.5]decan-8-ylcarboxamide)phenyl; 6-(3-methoxy-1,5-dioxa-9-azaspiro[5.5]undecan-9-yl)-3-pyridazinyl; 6-(1,5-dioxa-3-hydroxymethyl)-9-azaspiro[5.5]undecan-9-yl)-3-pyridazinyl; 6-(S-O-ethyl-2-hydroxymethyl)pyrrolidinyl)-3-pyridazinyl; 6-(4-acetyl-1-oxa-4,8-diazaspiro[4.5]decan-8-yl)-3-pyridazinyl; 6-(2(R,3R)-2,3-bis(methoxymethyl)-1,4-dioxa-8-azaspiro[4.5]decan-8-yl)-3-pyridazinyl; 6-(2(S,3S)-
25 2,3-dimethyl-1,4-dioxa-8-azaspiro[4.5]decan-8-yl)-3-pyridazinyl; 6-(4,4-(cis-1,2-dioxy)cyclopentane)piperidinyl)-3-pyridazinyl; 6-(4,4-(1S,2S-dimethoxymethyl)ethanediyo)piperidinyl)-3-pyridazinyl; 6-(4,4-(cis-3,4-dioxy-oxacyclopentane)piperidinyl)-3-pyridazinyl; 6-(4,4-(1,3-dioxy-2-methoxypropylene)piperidinyl)-3-pyridazinyl; 6-(4,4-(1,3-dioxy-2-
30 hydroxymethyl)propylene)piperidinyl)-3-pyridazinyl; 6-(4,4-(2-(2,2-spiro-

oxacyclopropane-1,3-dioxypropylene)piperidinyl)-3-pyridazinyl; 6-morpholinyl-3-pyridazinyl; 6-(4-morpholinyliminopiperidinyl)-3-pyridyl; 6-(4-(N-methylpiperazinyl)iminopiperidinyl)-3-pyridyl; 6-(4-(1,2,4-triazol-1-yl)iminopiperidinyl)-3-pyridyl; 6-(4-ethylpiperidinylcarboxylate)-3-pyridyl; 2-phenylmethyl-3(2H)-pyridazinone-6-yl; 6-(4-(morpholinylcarboxamide)piperidinyl)-3-pyridyl; 6-(4-(N,N-morpholinylaminocarboxamide)piperidinyl)-3-pyridyl; 6-(4-(N,N-dimethylaminocarboxamide)piperidinyl)-3-pyridyl; 6-(4-(N-methyl-N-methoxyethylcarboxamide)piperidinyl)-3-pyridyl; 6-(4-(N-methoxyethylcarboxamide)piperidinyl)-3-pyridyl; 6-(4-hydroxymethylpiperidinyl)-3-pyridyl; 6-(4-hydroxypiperidinyl)-3-pyridyl; 6-(4-N-acetyl(piperazinyl)-3-pyridyl; 6-(4-cyanopiperidinyl)-3-pyridyl; 6-(4-N-(4-fluorophenyl)piperazinyl)-3-pyridyl; 4-morpholinylbenzenesulfonamide; 4-N-4,4-ethylenedioxypiperidinylbenzenesulfonamide; 4-N-cyclopropylbenzenesulfonamide; 4-piperidinebenzenesulfonamide; 4-(4-cyanopiperidine)benzenesulfonamide; 4-N-cyclopropylmethylbenzenesulfonamide; 4-N,N-dimethylaminobenzenesulfonamide; 4-N-(S)-2-hydroxymethylpyrrolidinebenzenesulfonamide; 4-(4-hydroxypiperidine)benzenesulfonamide; 4-(cis-3,5-dimethylmorpholinyl)benzenesulfonamide; 3-fluoro-4-thiomorpholinylphenyl; 6-(thiomorpholinyl)-3-pyridyl; 6-(4,4-dioxothiomorpholinyl)-3-pyridyl; 4-(4,4-ethylenedioxypiperidinylcarboxamide)phenyl; 4-(N-cyclopropylcarboxamide)phenyl; 4-(morpholinylcarboxamide)phenyl; 6-N-cyclopropylamino-3-pyridyl; 4-(4-hydroxypiperidinylcarboxamide)phenyl; 6-(S)-hydroxymethylpyrrolidinyl-3-pyridazinyl; 6-(4-(2-ethoxyethoxy)piperidinyl)-3-pyridyl; 6-hexahydroypyrimidine)-3-pyridyl; 6-(S)-2-ethoxyethoxypyrrrolidinyl)-3-pyridyl; 6-(R)-2-ethoxyethoxypyrrrolidinyl)-3-pyridyl; 6-(cis-3,4-dihydroxypyrrrolidinyl)-3-pyridyl; 6-[(3aR,6aS)-tetrahydro-3aH-[1,3]dioxolo[4,5-c]pyrrol-2-one-5-yl]-3-pyridyl; 6-(cis-2,3-dihydroxypyrrrolidinyl)-3-pyridazinyl; 6-(S,R-2-hydroxymethyl-4-hydroxypyrrrolidinyl)-3-pyridyl; 6-(R-2-hydroxymethyl-4-pyrrolidinyl)-3-pyridazinyl; 6-(1S,4S)-2-aza-5-oxa-bicyclo[2.2.1]heptane)-3-pyridyl; 6-(2-imidizolidone-1-yl)-3-pyridyl; 4-(2,4-(1H,3H)-quinazolinedion-3-yl)phenyl; 6-morpholinylcarboxamide-3-pyridazinyl; 6-methoxy-3-pyridazinyl; 6-N,N-

diethoxyethylamino-3-pyridazinyl; 6-(4-ethoxymethylpiperidinyl)-3-pyridazinyl; 6-(4-(4-tetrahydropyranylmethyl)piperidinyl)-3-pyridazinyl; 6-(4-ethoxyethoxymethylpiperidinyl)-3-pyridazinyl; 6-N-methyl-N-1,3-dioxalanemethylamino)-3-pyridazinyl; 6-(4,4-dioxyethylenecyclohexyloxy)-3-pyridazinyl;

5 6-dihydroxymethylmethoxy-3-pyridazinyl; 6-(3-pyridyloxy)-3-pyridazinyl; 4,7-epoxy-7-methyl-2,3,3A,4,5,6,7,7a-octahydro-1H-isoindolyl; 6-(4-N-methyl-N-methoxyethyl)-3-pyridazinyl; 6-(3,4-dimethoxymethoxypyrrolidinyl)-3-pyridazinyl; 6-(trans-3-hydroxy-4-methylpyrrolidinyl)-3-pyridazinyl; 6-(trans-3-hydroxy-4-methylpyrrolidinyl)-3-pyridyl; 6-(cis-3-hydroxy-4-methylpyrrolidinyl)-3-pyridazinyl; 6-(cis-3-hydroxy-4-methylpyrrolidinyl)-3-pyridyl; 6-(trans-3-cyano-4-hydroxypyrrolidinyl)-3-pyridyl; 6-(3-hydroxy-4-tert-butylcarboxamidepyrrolidinyl)-3-pyridyl; 6-(S-2-(4-tetrahydropyranloxy)methylpyrrolidinyl)-3-pyridazinyl; 6-(2-(4-tetrahydropyranloxy)iminopyrrolidinyl)-3-pyridazinyl; 2-morpholinyl-5-thiazoyl; 5-bromo-2-thienyl; 2,5-dimethyl-3-thienyl; 5-chloro-2-thienyl; 2,4-dimethyl-5-thiazoyl; 5-

10 15 methyl-2-thienyl; 2-furanyl; 2-(4,4-dioxyethylenepiperidinyl)-5-thiazoyl; 3-thienyl; 3-methyl-2-thienyl; 2-morpholinyl-4-thiazoyl; 2-morpholinyl-4-trifluoromethyl-5-thiazoyl; 5-morpholinyl-2-thienyl; 4-methyl-2-morpholinyl-5-thiazoyl; 2,5-dichloro-3-thienyl; 2,5-dimethyl-3-furanyl; N-methyl-2-pyrrolyl; 2-N,N-dimethylamino-5-thiazoyl; 2-morpholinyl-5-thiazoyl; 2-(4,4-dioxythiomorpholinyl)-5-thiazoyl; 1-N-methyl-2-morpholinyl-5-imidazoyl; 2-morpholinyl-5-oxazoly; 2-N-methyl-N-methoxyethylamino-5-thiazoyl; 2-N-methyl-N-ethylamino-5-thiazoyl; 2-N-pyrrolidinyl-5-thiazoyl; 2-N-methyl-N-propylamino-5-thiazoyl; 2-N,N-diethylamino-5-thiazoyl; 2-(N-methylpiperazinyl)-5-thiazoyl; 2-(N-(2-pyridyl)piperazinyl)-5-thiazoyl; 2-N-methy-N-(2-pyridylethyl)-5-thiazoyl; 2-(4-oxopiperazinyl)-5-thiazoyl; 2-(4-(N-morpholinyl)iminopiperazinyl)-5-thiazoyl; 6-N-morpholine-3-pyridinesulfonamide; 2-(4-oxopiperidinyl)-5-pyrimidyl; 2-(4,4-dioxethylenepiperidinyl)-5-pyrimidyl; 5-(4,4-dioxethylenepiperidinyl)-2-pyrazinyl; 5-(4-oxopiperidinyl)-2-pyrazinyl; 6-N-cyclopropyl-3-pyridinesulfonamide; 6-N-(4,4-dioxethylenepiperidinyl)-3-pyridinesulfonamide; 2-(4-(4-tetrahydropyranloxy)iminopiperidinyl)-5-pyrazinyl; 6-(4-

20 25 30 (phenylmethoxy)iminopiperidinyl)-3-pyridyl; 6-(4-(tert-butylloxy)iminopiperidinyl)-3-

pyridyl; 6-(4-(cyclohexyloxy)iminopiperidinyl)-3-pyridyl; 6-(4-hydroxyiminopiperidinyl)-3-pyridyl; 6-(4-(4-tetrahydropyranloxy)iminopiperidinyl)-3-pyridyl; 6-(4-methoxyethoxyiminopiperidinyl)-3-pyridyl; 6-(4-(2-thenylmethoxy)iminopiperidinyl)-3-pyridyl; 6-(4-(4'-H-2-oxyfuranyl)-4-hydroxypiperidinyl)-3-pyridyl; 6-(4-(1-(4-tetrahydropyranloxy)iminoethyl)-4-hydroxypiperidinyl)-3-pyridazinyl; 6-(4-(4'-acetyl-4'-hydroxypiperidinyl)-3-pyridazinyl; 6-(4-(1-isopropylcarboxymethoxy)iminoethyl)-4-hydroxypiperidinyl)-3-pyridyl; 6-(4-(1-ethylcarboxymethoxy)iminoethyl)-4-hydroxypiperidinyl)-3-pyridyl; 6-(4-(1-methylcarboxymethoxy)iminoethyl)-4-hydroxypiperidinyl)-3-pyridyl; 6-(4-(1-(2-tetrahydropyranloxy)iminoethyl)-4-hydroxypiperidinyl)-3-pyridyl; 6-(4-(1-allyloxy)iminoethyl)-4-hydroxypiperidinyl)-3-pyridyl; 6-(4-(1-ethoxy)iminoethyl)-4-hydroxypiperidinyl)-3-pyridyl; 6-(4-(1-methoxy)iminoethyl)-4-hydroxypiperidinyl)-3-pyridyl; 6-(4-(1-hydroxy)iminoethyl)-4-hydroxypiperidinyl)-3-pyridyl; 6-(4-isopropylcarboxymethoxy)iminopiperidinyl)-3-pyridyl; 6-(4-hydroxy-4-(1-tetrahydropyranloxy)iminoethyl)-4-hydroxypiperidinyl)-3-pyridyl; 6-(4-(3-butyrolactone)-4-hydroxypiperidinyl)-3-pyridyl; 6-(4-(2-butyrolactone)-4-hydroxypiperidinyl)-3-pyridazinyl; 6-(4-acetyl-4-hydroxypiperidinyl)-3-pyridyl; 6-(3-hydroxyazetidinyl)-3-pyridyl; 6-(cis-3-hydroxytropanyl)-3-pyridyl; 6-(cis-2,3-dihydroxypiperidinyl)-3-pyridyl; 6-(N-methyl-N-(3-pyridylmethyl)amino)-3-pyridazinyl; 6-(1,2,3,6-tetrahydropyridyl)-3-pyridyl; 6-(4-(N-4'-methoxyphenylcarbamoyl)piperidinyl)-3-pyridazinyl; 6-(4-(2-butyrolactone)-4-hydroxypiperidinyl)-3-pyridyl; 6-(trans-3,4-bis(N-4'-methoxyphenylcarbamoyl)pyrrolidinyl)-3-pyridyl; 6-(trans-3-hydroxytropanyl)-3-pyridyl; 6-(S,S-trans-3,4-dihydroxypyrrrolidinyl)-3-pyridyl; 6-(R,R-trans-3,4-dihydroxypyrrrolidinyl)-3-pyridyl; 6-(8-(1-phenyl-1,3,8-triaza-2-spiro[4,5]deceN-4-one)-3-pyridyl; 6-(8-(1-phenyl-1,3,8-triaza-2-spiro[4,5]deceN-4-one)-3-pyridyl; 6-(4-(2-keto-1-benzimidazolinyl)piperidinyl)-3-pyridazinyl; 6-(4-oxothiomorpholinyl)-3-pyridyl; 6-(4-(2-keto-1-benzimidazolinyl)piperidinyl)-3-pyridyl; 6-(N-methyl-N-(2-pyridylethyl)amino)-3-pyridyl; 6-(N-methyl-N-(4-pyridylethyl)amino)-3-pyridyl; 6-(N-(3-pyridylmethyl)amino)-3-pyridyl; 6-(2-hydroxymethylpiperidinyl)-3-pyridyl; 6-(4-hydroxy-4-(4-

bromophenyl)piperidinyl)-3-pyridyl; 6-(4-N-(2-pyridnyl)piperazinyl)-3-pyridyl; 6-(4-N-(2-hydroxyethoxyethyl)piperazinyl)-3-pyridyl; 6-(4,4-diacetoxymethylthio)piperidinyl)-3-pyridyl; 6-(N-methyl-N-(3-pyridylmethyl)amino)-3-pyridyl; 6-(4-pyrrolidinyl)piperidinyl)-3-pyridyl; 6-(4-N-cyanomethylpiperazinyl)-3-pyridyl; 6-(3-hydroxypyrrrolidinyl)-3-pyridyl;

5 6-(4-methylpiperidinyl)-3-pyridyl; 6-(cis-3,5-dimethylmorpholinyl)-3-pyridyl; 6-(4,4-difluoropipridinyl)-3-pyridyl; 6-(4,4-dioxothiomorpholinyl)-3-pyridazinyl; 6-thiazolidinyl-3-pyridyl; 6-(1,1-dioxothiazolidinyl)-3-pyridyl; 6-thiomorpholinyl-3-pyridazinyl; 6-(2,5-dihydropyrrrolyl)-3-pyridyl; 6-hydroxy-3-pyridazinyl; 6-piperidinyl-3-pyridyl; and 6-(4-tetrahydropyranloxy)iminopyrrolidinyl-3-pyridyl; 6-morpholinyl-3-pyridyl.

13. A compound according to claim 10 wherein R³ is selected from the group consisting of:

(thiophene-2-yl)methyl; (thiophene-3-yl)methyl; butyl; cycloheptyl; pentyl;

15 thiophene-2-yl; 1-(3-bromophenyl)ethyl; 2-(N-phenylmethoxycarbonyl)aminophenyl; 2-(3-bromophenyl)ethyl; 2-(3-cyanophenyl)methyl; 2-(4-bromophenyl)ethyl; 2-(5-chloro-2-thiophen-3-yl)phenyl; 2-bromophenyl; 2-furanyl; 2-methylpropyl; 2-phenylethyl; phenylmethyl; 2,3-dimethoxyphenyl; 2,3-methylenedioxyphenyl; 3-(furan-2-yl)phenyl; 3-(thiophen-2-yl)phenyl; 3-(2-pyridyl)phenyl; 3-(3-methoxybenzyl)phenyl; 2-(3-aminopropynyl)phenylmethyl; 3-benzylxyphenyl; 3-bromo-4-fluorophenyl; 3-bromo-5-iodophenyl; 3-bromo-5-methoxyphenyl; 3-bromophenyl; 3-bromophenyl)methyl; 3-carboxamidophenyl; 3-chlorophenyl; 3-cyanophenyl; 3-diethylmalonylallylphenyl; 3-dimethylaminophenyl; 3-ethoxyphenyl; 3-fluoro-5-trifluoromethylphenyl; 3-fluorophenyl; 3-hydroxyphenyl; 3-iodophenyl; 3-methoxyethoxyphenyl; 3-methoxyphenyl; 3-

20 methylphenyl; 3-methylsulfonylphenyl; 3-methylthiophenyl; 3-t-butylacrylphenyl; 3-trifluoromethoxyphenyl; 3-trifluoromethylphenyl; 3-vinylpyridinylphenyl; 3,4,5-dichlorophenyl; 3,4-dimethoxyphenyl; 3,4-methylenedioxyphenyl; 3,4,5-trimethoxyphenyl; 3,5-di(trifluoromethyl)phenyl; 3,5-dibromophenyl; 3,5-dichlorophenyl; 3,5-dimethoxyphenyl; 3,5-dimethylphenyl; 4-(2-propyl)phenyl; 4-(2-propyl)oxyphenyl; 4-

25 benzylxyphenyl; 4-bromophenyl; 4-bromothiophene-2-yl; 4-butoxyphenyl; 4-

30

dimethylaminophenyl; 4-fluoro-3-trifluoromethylphenyl; 4-methoxyphenyl; 4-neopentylphenyl; 4-phenoxyphenyl; 5-bromothiophene-2-yl; 5-cyclohexyl; 5-cyclopropyl; 5-hexyl; 5-methyl; 5-phenyl; (2-bromo-5-chlorophenyl)methyl; (2-bromophenyl)methyl; (5-chloro-2-(3-methoxyphenyl)phenyl)methyl; 3-bromophenyl; 2-pyridyl; 2-ethoxyphenyl; 5-ethoxyphenyl; 2,5-dichlorophenyl; 2,5-dimethylphenyl; 3-fluorophenyl; 3-trifluoromethylphenyl; 5-trifluoromethylphenyl; 3,5-diclorophenyl; 4-bromo-2-thienyl; 3-bromo-2-thienyl; 3-cyanophenyl; 4-tetrahydropyranyl; 3-indolyl; 5-indolyl; 4-quinolyl; 2-bromophenyl; 4-fluorophenyl; 4,4-difluorocyclohexyl; 1,1-dimethyl-3-butenyl; 2,3-dichlorophenyl; isopropyl; and 2-trifluorophenylphenyl.

10 14. A compound according to claim 10 selected from the group consisting of:
4-(N-(2,3-dihydroxypropyl)amino)-5-(3-bromophenyl)-7-(6-morpholinyl-3-pyridinyl)pyrido[2,3-d]pyrimidine;
4-(N-(3-morpholinylpropyl)amino)-5-(3-bromophenyl)-7-(6-morpholinyl-3-pyridinyl)pyrido[2,3-d]pyrimidine;
4-(N-(2-(4-imidazolyl)ethyl)amino)-5-(3-bromophenyl)-7-(6-morpholinyl-3-pyridinyl)pyrido[2,3-d]pyrimidine;
4-(N-(3-carboxypropyl)amino)-5-(3-bromophenyl)-7-(6-morpholinyl-3-pyridinyl)pyrido[2,3-d]pyrimidine;
20 (S)-4-amino-5-(3-bromophenyl)-7-(6-(O-methyl-2-hydroxymethylpyrrolidinyl)-3-pyridinyl)pyrido[2,3-d]pyrimidine;
(S)-4-amino-5-(3-bromophenyl)-7-(6-(2-hydroxymethylpyrrolidinyl)-3-pyridinyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(2-bromophenyl)-7-(6-(4-hydroxypiperidinyl)-3-pyridinyl)pyrido[2,3-d]pyrimidine;
25 4-amino-5-(4-fluorophenyl)-7-(6-(4,4-ethylenedioxypiperidinyl)-3-pyridinyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(2-bromophenyl)-7-(6-(4-hydroxypiperidinyl)-3-pyridazyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4,4-ethylenedioxy piperidinyl)-3-pyridazyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(2-morpholinyl-4-thiazolyl)pyrido[2,3-d]pyrimidine;

5 4-amino-5-(N-methyl-3-indolyl)-7-(6-morpholinyl-3-pyridinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-ethoxyiminopiperidinyl)-3-pyridinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-ethoxycarbonylmethoxyiminopiperidinyl)-3-pyridinyl)pyrido[2,3-d]pyrimidine;

10 4-amino-5-(4-dimethylaminophenyl)-7-(4-bromophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(4-dimethylaminophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(4-methoxyphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

15 4-amino-5-(4-dimethylaminophenyl)-7-(4-methoxyphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(4-(2-propyl)phenyl)-7-(4-methoxyphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(4-neopentylphenyl)-7-(4-methoxyphenyl)pyrido[2,3-d]pyrimidine;

20 4-amino-5-(4-butoxyphenyl)-7-(4-methoxyphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(4-methoxyphenyl)-7-(4-bromophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(4-(2-propyl)oxyphenyl)-7-(4-methoxyphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(4-butoxyphenyl)-7-(4-N-formylpiperazinylphenyl)pyrido[2,3-d]pyrimidine;

25 4-amino-5-(4-benzyloxyphenyl)-7-(4-methoxyphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(4-phenoxyphenyl)-7-(4-methoxyphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(4-(2-propyl)phenyl)-7-(4-diethylmalonylallylphenyl)pyrido[2,3-d]pyrimidine;

30 4-amino-5-(4-(2-propyl)phenyl)-7-(4-t-butylacetylphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3,4-dimethoxyphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-t-butylacrylphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

5 4-amino-5-(3-methoxyphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3,5-dimethoxyphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-diethylmalonylallylphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

10 4-amino-5-(3-vinylpyridinylphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-trifluoromethylphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-carboxamidophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

15 4-amino-5-(3-cyanophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-benzyloxyphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-methoxyphenyl)-7-(4-methoxyphenyl)pyrido[2,3-d]pyrimidine;

20 4-amino-5-(3-bromophenyl)-7-(4-butoxyphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-(2-pyridyl)phenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-methylphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-chlorophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

25 4-amino-5-(3-fluorophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-methoxyphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-methoxyphenyl)-7-(4-bromophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-phenylpyrido[2,3-d]pyrimidine;

30 4-amino-5-(3-bromophenyl)-7-(4-ethylphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-bromophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-cyanophenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3-bromophenyl)-7-(4-hydroxyphenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3-iodophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3-ethoxyphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;
5 4-amino-5-(3-trifloromethoxyphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3,5-dichlorophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;
10 4-amino-5-(3-bromo-4-fluorophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3-hydroxyphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3-bromophenyl)-7-(4-morpholinylphenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3-bromophenyl)-7-(4-piperidinylphenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3-bromophenyl)-7-(4-imidazol-1-yl)phenyl)pyrido[2,3-d]pyrimidine;
15 4-amino-5-(3-bromophenyl)-7-(4-chlorophenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3-bromophenyl)-7-(4-isopropylphenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3-bromophenyl)-7-(4-trifluorophenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3-bromophenyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3-bromophenyl)-7-(3,4,5-trimethoxyphenyl)pyrido[2,3-d]pyrimidine;
20 4-amino-5-(3-(3-methoxybenzyl)phenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3-methoxyethoxyphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3,4-methylenedioxyphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;
25 4-amino-5-(3-bromophenyl)-7-(4-ethoxyphenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3-bromophenyl)-7-(2'-thiophene)pyrido[2,3-d]pyrimidine;
4-amino-5-(3-bromophenyl)-7-(4-fluorophenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3-dimethylaminophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-phenyl-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3,4,5-trimethoxyphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-
d]pyrimidine;

5 4-amino-5-(3-bromophenyl)-7-(4-nitrophenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3-bromophenyl)-7-(4-iodophenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3-bromophenyl)-7-(3,4-methylenedioxophenyl)pyrido[2,3-
d]pyrimidine;

10 4-amino-5-(thiophen-2-yl)-7-(4-morpholinylphenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3,5-dimethoxyphenyl)-7-(thiophen-2-yle)pyrido[2,3-d]pyrimidine;
4-amino-5-(3-bromophenyl)-7-(4-carboxamidophenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3-bromophenyl)-7-(4-(2-methoxy)ethoxyphenyl)pyrido[2,3-
d]pyrimidine;

15 4-amino-5-(3,5-dimethoxyphenyl)-7-(4-morpholinylphenyl)pyrido[2,3-
d]pyrimidine;
4-amino-5-(3-trifluoromethylphenyl)-7-(thiophene-2-yl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3-bromophenyl)-7-(4-aminophenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3-bromo-4-fluorophenyl)-7-(thiophene-2-yl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3-bromo-4-fluorophenyl)-7-(2-furanyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3,5-dimethoxyphenyl)-7-(4-iodophenyl)pyrido[2,3-d]pyrimidine;

20 4-amino-5-(3,5-dimethoxyphenyl)-7-(4-imidazolylphenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3,5-dimethoxyphenyl)-7-(4-(thiophene-2-yl)phenyl)pyrido[2,3-
d]pyrimidine;

25 4-amino-5-(3,5-dimethoxyphenyl)-7-(4-(3-pyridyl)phenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3-bromophenyl)-7-(4-(4-methylpiperidinyl)phenyl)pyrido[2,3-
d]pyrimidine;

30 4-amino-5-(3-bromophenyl)-7-(4-pyrrolidinylphenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(4-bromothiophene-2-yl)-7-(4-dimethylaminophenyl)pyrido[2,3-
d]pyrimidine;

4-amino-5-(4-bromothiophene-2-yl)-7-(4-morpholinylphenyl)pyrido[2,3-
d]pyrimidine;

4-morpholiny-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(5-bromo-2-yl)-7-(4-morpholinyphenyl)pyrido[2,3-d]pyrimidine;

5 4-amino-5-(4-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(acetylamino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3,5-dimethoxyphenyl)-7-(5-pyrimidinylphenyl)pyrido[2,3-d]pyrimidine;

10 4-(4-fluorophenyl)amino-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(4-bromo-2-yl)-7-(4-pyrrolidinylphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(4-bromo-2-yl)-7-(thiophene-2-yl)pyrido[2,3-d]pyrimidine;

15 4-amino-5-(3-bromophenyl)-7-(5-(dimethylamino)thiophene-2-yl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromo-5-iodophenyl)-7-(4-(dimethylamino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3,5-di(trifluoromethyl)phenyl)-7-(4-(dimethylamino)phenyl)pyrido[2,3-d]pyrimidine;

20 4-amino-5-(3,5-di(trifluoromethyl)phenyl)-7-(4-morpholinyphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3,5-dibromophenyl)-7-(4-(dimethylamino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3,5-dibromophenyl)-7-(4-(dimethylamino)phenyl)pyrido[2,3-d]pyrimidine;

25 4-amino-5-(3,5-dibromophenyl)-7-(4-morpholinyphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(4-bromo-2-yl)-7-(4-(4-methylpiperidinyl)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3,5-dibromophenyl)-7-(4-(dimethylamino)phenyl)pyrido[2,3-d]pyrimidine;

30 4-amino-5-(3-bromophenyl)-7-(3-(dimethylamino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-methylsulfonylphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(3-methoxyphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(methylthio)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(3,4-dichlorophenyl)pyrido[2,3-d]pyrimidine;

5 4-amino-5-(3-bromophenyl)-7-(4-(N-methyl-N-formylamino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-methylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromo-4-fluorophenyl)-7-(4-methylsulfonylphenyl)pyrido[2,3-d]pyrimidine;

10 4-amino-5-(3-bromophenyl)-7-(3-amino-4-methoxyphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(3-bromo-4-(dimethylamino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(3-methyl-4-(dimethylamino)phenyl)pyrido[2,3-d]pyrimidine;

15 4-amino-5-(3-bromophenyl)-7-(4-(N-methyl-N-trifluoroacetylamino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(dimethylamino)-3-fluorophenyl)pyrido[2,3-d]pyrimidine;

20 4-amino-5-(3-bromophenyl)-7-(4-(N-ethyl-N-formylamino)phenyl)pyrido[2,3-d]pyrimidine;

4,4-bis(acetylamino)-5-(3-bromophenyl)-7-(4-(N-methyl-N-acetylamino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(N-acetyl-N-methylamino)phenyl)pyrido[2,3-d]pyrimidine;

25 4-amino-5-(3-bromophenyl)-7-(4-(N-ethylamino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(N-methyl-N-(2-methoxyethyl)amino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(N-isopropylamino)phenyl)pyrido[2,3-d]pyrimidine;

30 4-amino-5-(3-bromophenyl)-7-(4-(N-isopropylamino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-N-ethyl-N-(2-methoxyethyl)amino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-N-(3-methoxypropionyl)-N-isopropylamino)phenyl)pyrido[2,3-d]pyrimidine;

5 4-amino-5-(3-bromophenyl)-7-(4-N-(2-(dimethylamino)ethyl)-N-formylamino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(N-(2-(dimethylamino)ethyl)amino)phenyl)pyrido[2,3-d]pyrimidine;

10 4-amino-5-(3-bromophenyl)-7-(4-(N-methyl-N-(2-cyano)ethyl)amino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(N-methyl-N-(3-methoxy)propionylamino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(3-methyl-4-(N-formyl-N-methylamino)phenyl)pyrido[2,3-d]pyrimidine;

15 4-amino-5-(3-bromophenyl)-7-(3-methyl-4-(N-methylamino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(4-methoxy-2-butyl)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(N-methyl-N-(2-phthalimidyl)acetyl)amino)phenyl)pyrido[2,3-d]pyrimidine;

20 4-amino-5-(3-bromophenyl)-7-(3-methyl-4-(N-methyl-N-(trifluoroacetyl)amino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(3-methyl-4-(N-acetyl-N-methylamino)phenyl)pyrido[2,3-d]pyrimidine;

25 4-amino-5-(3-bromophenyl)-7-(6-dimethylamino-3-pyridinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-cyanophenyl)-7-(4-methylsulfonylphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-cyanophenyl)-7-(4-(N-methyl-N-formylamino)-phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(N-methyl-N-formylamino)-3-pyridinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-morpholiny-3-pyridinyl)pyrido[2,3-d]pyrimidine;

5 4-amino-5-(3-bromophenyl)-7-(6-(N-methyl-N-methoxyethylamino)-3-pyridinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-pyrrolidinyl-3-pyridinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(2-(dimethylamino)-5-pyrimidinyl)pyrido[2,3-d]pyrimidine;

10 4-amino-5-(3-bromophenyl)-7-(2-(N-methoxyethyl-N-methyl amino)-5-pyrimidinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(2-(N-formyl-N-methyl amino)-5-pyrimidinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(2-(N-methylamino)5-pyrimidinyl)pyrido[2,3-d]pyrimidine;

15 4-amino-5-(3-bromophenyl)-7-(2-(1-pyrrolidinyl)-5-pyrimidinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(2-(1-morpholiny)-5-pyrimidinyl)pyrido[2,3-d]pyrimidine;

20 4-amino-5-(3-bromophenyl)-7-(6-(2-oxo-3-oxazolidinyl)-3-pyridinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(2-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(3-pyridyl)pyrido[2,3-d]pyrimidine;

25 4-amino-5-(3-(thiophen-2-yl)phenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-(furan-2-yl)phenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-(3-methoxyphenyl)phenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

30 4-amino-5-phenyl-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-chlorophenyl)-7-(4-(morpholinyl)phenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3-bromo-4-fluorophenyl)-7-(4-(morpholinyl)phenyl)pyrido[2,3-d]pyrimidine;

5 4-amino-5-(3-chlorophenyl)-7-(4-(thiophen-2-yl)phenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3-chlorophenyl)-7-(4-(5-pyrimidinyl)phenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3-bromo-4-fluorophenyl)-7-(4-iodophenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(4-bromothiophene-2-yl)-7-(4-methoxyphenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3-bromophenyl)methyl-7-(4-(dimethylamino)phenyl)pyrido[2,3-d]pyrimidine;

10 4-amino-5-(2-phenylethyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(2-methylpropyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(butyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(2-(4-bromophenyl)ethyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine;

15 4-amino-5-(butyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(2-(3-cyanophenyl)methyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(2-(N-phenylmethoxycarbonyl)aminoethyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

20 4-amino-5-(cycloheptyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(2-(5-chloro-2-(thiophen-3-yl)phenyl)methyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

25 4-amino-5-(pentyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-hexyl-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(2-(3-bromophenyl)ethyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine;

30 4-amino-5-((2-bromophenyl)methyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-cyclopropyl-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-((2-bromo-5-chlorophenyl)methyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-methyl-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine;

5 4-amino-5-(2,3-methylenedioxyphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-fluoro-5-trifluoromethylphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(2-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

10 4-amino-5-(3,5-dimethylphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3,4-dichlorophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(4-fluoro-3-trifluoromethylphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

15 4-amino-5-(3-bromo-5-methoxyphenyl)-7-(4-morpholinylphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromo-5-methoxyphenyl)-7-(4-pyrrolidinylphenyl)pyrido[2,3-d]pyrimidine;

20 4-amino-5-(3-bromo-5-methoxyphenyl)-7-(4-piperidinylphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromo-5-methoxyphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-methylthiophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

25 4-amino-5-(3-bromo-5-methoxyphenyl)-7-(thiophene-2-yl)pyrido[2,3-d]pyrimidine;

4-amino-5-(2,3-dimethoxyphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-methylsulfonylphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

30 4-amino-5-(3-methylsulfonylphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-acetylamino-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-formylamino-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

5 4-(methoxyacetyl)amino-5-(3-bromophenyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-trifluoroacetylamino-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-pentanoylamino-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

10 4-benzoylamino-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-(N-BOC-glycyl)amino-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

15 4-(N-phthalimidylglycyl)amino-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-(ethoxycarbonyl)amino-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-(ethylaminocarbonyl)amino-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

20 4-allylamino-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-(2-(N,N-dimethylamino)ethylamino)-5-(4-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

25 4-(4-(N,N-dimethylamino)butylamino)-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-(N-allyl-N-formylamino)-5-(4-dimethylaminophenyl)-7-(4-bromophenyl)pyrido[2,3-d]pyrimidine;

30 4-diacetylamino-5-(p-dimethylaminophenyl)-7-(4-bromophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(5-amino-2-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(5-dimethylamino-2-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(5-dimethylamino-2-pyrazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(2-oxobenzoxazolin-6-yl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(1-methyl-2-oxobenzoxazolin-6-yl)pyrido[2,3-d]pyrimidine;

4-amino-5-((5-chloro-2-(3-methoxyphenyl)phenyl)methyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-((thiophene-2-yl)methyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-((thiophene-3-yl)methyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-((2-bromophenyl)methyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(N-formyl-N-(2-methoxyethyl)amino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(N-(2-methoxyethyl)amino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(N-methyl-N-(2-dimethylamino)ethyl)amino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(2-methoxy)acetylamino)ethyl)amino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-((4-formylamino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(2-(dimethylamino)acetylamino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(2-oxo-3-oxazolidinyl)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(2-propyl)-3-pyridinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(3-methyl-4-pyrrolidinylphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-imidazolyl-3-pyridinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-phenylmethyl-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine;

5 4-amino-5-(2-(3-aminopropynyl)phenylmethyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(1-(3-bromophenyl)ethyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine;

10 4-amino-5-(4-dimethylaminophenyl)-7-(4-bromophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(2-furanyl)-7-(4-(N-morpholinyl)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(2-dimethylamino-5-pyrimidinyl)pyrido[2,3-d]pyrimidine;

15 4-amino-5-(3-bromophenyl)-7-(4-(ureido)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(1-phenylmethyl-3-piperidinyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(3-methyl-5-isoxazolyl))-3-pyridinyl)pyrido[2,3-d]pyrimidine;

20 4-amino-5-(3-bromophenyl)-7-(6-chloro-3-pyridinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-methoxy-3-pyridinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(1,2,4-triazol-4-yl)-3-pyridinyl)pyrido[2,3-d]pyrimidine;

25 4-amino-5-(3-bromophenyl)-7-(2-morpholinyl-5-pyrimidinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(2-thiazolyl)-7-(4-pyrrolidinylphenyl)-pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-pyrazolyl-3-pyridinyl)-pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(1-methyl-ureido)phenyl)-pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(N-methyl-N-(2-pyrimidinyl)amino)phenyl)-pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(3-fluoro-4-(N-formyl-N-methylamino)phenyl)-pyrido[2,3-d]pyrimidine;

5 4-formylamino-5-(3-bromophenyl)-7-(3-fluoro-4-(N-formyl-N-methylamino)phenyl)-pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(N-methyl-N-methylsulfonylamino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(N-methyl-N-methylsulfonylamino)-3-pyridinyl)pyrido[2,3-d]pyrimidine;

10 4-amino-5-(3-bromophenyl)-7-(1-methyl-5-indolinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(1-methyl-5-benzimidazolyl)pyrido[2,3-d]pyrimidine;

15 4-amino-5-(3-bromophenyl)-7-(6-dimethylamino-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3bromophenyl)-7-(6-morpholinyl-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-pyrrolidinyl-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

20 4-amino-5-(3-bromophenyl)-7-(5-morpholinyl-2-pyrazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(5-(N-(2-methoxyethyl)-N-methylamino)-2-pyrazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(morpholinylmethyl)-phenyl)pyrido[2,3-d]pyrimidine;

25 4-amino-5-(3-bromophenyl)-7-(5-(N,N-bis(2-methoxyethyl)amino)-2-pyridinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(imidazolylmethyl)-phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(5-(1-morpholinyl)-2-pyridinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-((dimethylamino)methyl)-phenyl)pyrido[2,3-d]pyrimidine;

5 4-amino-5-(3-bromophenyl)-7-(5-(4-hydroxy-1-piperidinyl)-2-pyridinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(5-(N-formyl-N-methylamino)-2-pyridinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(5-(2-propenyl)-2-pyridinyl)pyrido[2,3-d]pyrimidine;

10 4-amino-5-(3-bromophenyl)-7-(3-(2-methoxyethyl)-2-oxo-6-benzoxazolyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(1-(N-formylamino)-ethyl)phenyl)pyrido[2,3-d]pyrimidine;

15 4-(methylamino)-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine hydrochloride;

4-(2-methoxyethylamino)-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine hydrochloride;

4-amino-5-(3-bromophenyl)-7-(4-(1-methyl-2-imidazolyl)phenyl)pyrido[2,3-d]pyrimidine trihydrochloride;

20 4-amino-5-(3-bromophenyl)-7-(4-(aminomethyl)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(2-bromo-4-(dimethylamino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(dimethylaminoethyl)phenyl)pyrido[2,3-d]pyrimidine;

25 4-amino-5-(3-bromophenyl)-7-(4-(3-(dimethylamino)propynyl)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(3-amino-3-methylbutynyl)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-dimethylphosphonatophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(3-(methoxypropynyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-carboxyphenyl)pyrido[2,3-d]pyrimidine;

5 4-amino-5-(3-bromophenyl)-7-(4-methyl-3-oxo-2H-4H-pyrido[3,2-b]-1,4-oxazin-7-yl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(2-(dimethylamino)ethyl)-3-oxo-2H-4H-pyrido[3,2-b]-1,4-oxazin-7-yl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(2,3-dihydro-3-(dimethylaminoethyl)-2-10 oxobenzoxazol-6-yl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-methyl-3-oxo-2H-4H-benzo-1,4-oxazin-7-yl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(2,2,4-trimethyl-3-oxo-2H-4H-benzo-1,4-oxazin-7-yl)pyrido[2,3-d]pyrimidine;

15 4-amino-5-cyclohexyl-7-(4-(2-dimethylamino)ethyl)-2H-4H-benzo-3-oxo-1,4-oxazin-7-yl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(5-(1-methylethyl)-2-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(5-piperidin-1-ylpyrid-2-yl)pyrido[2,3-20 d]pyrimidine;

4-amino-5-(1-(4-bromophenyl)ethyl)-7-(6-morpholinylpyrid-3-yl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-((N-formylamino)methyl)phenyl)pyrido[2,3-d]pyrimidine;

25 4-amino-5-(3-bromophenyl)-7-(4-(1-methyl-1-(N-methylamino)ethyl)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(1-(dimethylamino)-1-methylethyl)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(N-acetyl-5-indolinyl)pyrido[2,3-d]pyrimidine;

30 4-amino-5-cyclohexyl-7-(6-chloro-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(1-(2-bromophenyl)ethyl)-7-(6-diethylamino-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(1-(2-bromophenyl)ethyl)-7-(6-morpholiny-3-pyridyl)pyrido[2,3-d]pyrimidine;

5 4-amino-5-(1-(2-bromophenyl)ethyl)-7-(4-(N-methyl-N-formyl)amino)-phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(6-morpholiny-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-((2-bromophenyl)methyl)-7-(6-morpholiny-3-pyridyl)pyrido[2,3-d]pyrimidine;

10 4-amino-5-(4-tetrahydropyranyl)-7-(6-morpholiny-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(6-dimethylamino-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(1-ethylpropyl)-7-(6-dimethylamino-3-pyridyl)pyrido[2,3-d]pyrimidine;

15 4-amino-5-cyclopentyl-7-(6-morpholiny-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(2-chloro-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3,5-dimethylcyclohexyl)-7-(6-dimethylamino-3-pyridyl)pyrido[2,3-d]pyrimidine;

20 4-amino-5-((N-(benzyloxycarbonyl)-4-piperidinyl)methyl)-7-(6-morpholiny-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(6-bromo-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(3-cyanophenyl)pyrido[2,3-d]pyrimidine;

25 4-amino-5-(1-(2-bromophenyl)ethyl)-7-(6-dimethylamino-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-imidazolyl-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(azacycloheptanyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(N-methyl-N-(1-methylethyl))amino)-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(1-(2-bromophenyl)ethyl)-7-(6-morpholiny1-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(6-(4-acetyl piperazinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

5 4-amino-5-cyclohexyl-7-(6-(4-acetyl-1,4-diazacycloheptanyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(6-(4-methyl-1,4-diazacycloheptanyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

10 4-amino-5-cyclohexyl-7-(6-(N-methyl-N-(2-(2-pyridyl)ethyl)amino)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(6-2-(N-(N',N'-dimethylaminoethyl)-N-methylamino)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(6-azetidinyl-3-pyridyl)pyrido[2,3-d]pyrimidine;

15 4-amino-5-cyclohexyl-7-(6-(3-(N-methylacetamido)pyrrolidinyl)pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(6-(3-(formamido)pyrrolidinyl)pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(4-oxo-1-phenyl-1,3,8-triazaspiro[4.5]decan-8-yl)pyrido[2,3-d]pyrimidine;

20 4-amino-5-cyclohexyl-7-(6-(2-methoxymethyl)pyrrolidin-1-yl)pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(6-(N-methoxyethyl-N-propylamino)pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(N-methyl-N-(2,2-dimethoxyethyl)amino)pyrido[2,3-d]pyrimidine;

25 4-amino-5-cyclohexyl-7-(6-(4-(dimethylamino)piperidinyl)pyridyl)pyrido[2,3-d]pyrimidinc;

4-amino-5-cyclohexyl-7-(6-(4-(aminocarbonyl))piperidinyl)pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(N-methyl-N-(3-(diethylamino)propyl)aminopyrid-3-yl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(6-(N-methyl-N-(4-pyridyl)ethylamino)pyrid-3-yl)pyrido[2,3-d]pyrimidine;

5 4-amino-5-cyclohexyl-7-(6-(N-methyl-N-(3-pyridylmethylamino)pyrid-3-yl)pyrido[2,3-d]pyrimidine;

4-amino-5-(1-(2-bromophenyl)ethyl)-7-(1-methyl-5-indolyl)pyrido[2,3-d]pyrimidine;

10 4-amino-5-(1-(2-bromophenyl)ethyl)-7-(1-methyl-2,3-dioxo-5-indolyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(3-fluoro-4-(1-morpholinyl)phenyl)pyrido[2,3-d]pyrimidine;

15 4-amino-5-(3-bromophenyl)-7-(4-hydroxy-3-nitrophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4,4-ethylenedioxypiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-oxopiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

20 4-amino-5-(3-bromophenyl)-7-(6-(4-methylpiperazinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-formylpiperazinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-thiomorpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidin;

25 4-amino-5-(3-bromophenyl)-7-(6-(4,4-dioxothiomorpholinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(2-bromophenyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromo-4-methoxyphenyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine;

30 4-amino-5-(4-bromophenyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-chlorophenyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(5-chloro-6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(N-oxidomorpholinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

5 4-amino-5-(3-bromophenyl)-7-(6-(N-(2-hydroxyethoxyethyl)amino)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(N-(2-hydroxyethoxyethyl)-N-formylamino)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(N-(2-hydroxyethoxyethyl)-3-pyridyl-N-oxide)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(3-hydroxy)morpholinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

10 1-(5-(4-amino-5-(3-bromophenyl)pyrido[2,3-d]pyrimidin-7-yl)-2-pyridyl)-piperidine-4-phosphate, disodium salt;

15 4-amino-5-(3-bromophenyl)-7-(4-methylenylpiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-hydroxy-4-(hydroxymethyl)piperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4,4-ethylenedioxypiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

20 4-amino-5-cyclohexyl-7-(6-(4-oxo-piperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(6-(4-methylenylpiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-N-(iminomethyl)amino-5-cyclohexyl-7-(6-dimethylamino-3-pyridyl)pyrido[2,3-d]pyrimidine;

25 4-allylamino-5-(4-bromophenyl)-7-(4-dimethylaminophenyl) pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-hydroxypiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(cyclohexyl)-7-(6-(4,4-ethylenedioxypiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(2-morpholinyl-5-thiazolyl)pyrido[2,3-d]pyrimidine;

5 4-(N-(2,3-dihydroxypropyl)amino)-5-(3-bromophenyl)-7-(6-morpholinyl-3-pyridinyl)pyrido[2,3-d]pyrimidine;

4-(N-(3-morpholinylpropyl)amino)-5-(3-bromophenyl)-7-(6-morpholinyl-3-pyridinyl)pyrido[2,3-d]pyrimidine;

4-(N-(2-(4-imidazolyl)ethyl)amino)-5-(3-bromophenyl)-7-(6-morpholinyl-3-pyridinyl)pyrido[2,3-d]pyrimidine;

10 4-(N-(3-carboxypropyl)amino)-5-(3-bromophenyl)-7-(6-morpholinyl-3-pyridinyl)pyrido[2,3-d]pyrimidine;

(S)-4-amino-5-(3-bromophenyl)-7-(6-(O-methyl-2-hydroxymethylpyrrolidinyl)-3-pyridinyl)pyrido[2,3-d]pyrimidine;

15 (S)-4-amino-5-(3-bromophenyl)-7-(6-(2-hydroxymethylpyrrolidinyl)-3-pyridinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(2-bromophenyl)-7-(6-(4-hydroxypiperidinyl)-3-pyridinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(4-fluorophenyl)-7-(6-(4,4-ethylenedioxypiperidinyl)-3-pyridinyl)pyrido[2,3-d]pyrimidine;

20 4-amino-5-(2-bromophenyl)-7-(6-(4-hydroxypiperidinyl)-3-pyridazyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4,4-ethylenedioxypiperidinyl)-3-pyridazyl)pyrido[2,3-d]pyrimidine;

25 4-amino-5-(3-bromophenyl)-7-(2-morpholinyl-4-thiazolyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(N-methyl-3-indolyl)-7-(6-morpholinyl-3-pyridinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-ethoxyiminopiperidinyl)-3-pyridinyl)pyrido[2,3-d]pyrimidine;

30 4-amino-5-(3-bromophenyl)-7-(6-(4-ethoxyiminopiperidinyl)-3-pyridinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-ethoxycarbonylmethoxyiminopiperidinyl)-3-pyridinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-oxopiperidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

5 4-amino-5-(3-bromophenyl)-7-(6-(4-morpholinyliminopiperidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptan-5-yl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-methoxyiminopiperidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

10 4-amino-5-(3-bromophenyl)-7-(6-phenylmethoxy-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-methoxypiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-(4-tetrahydropyranloxy)iminopiperidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

15 4-amino-5-(3-bromophenyl)-7-(6-isobutoxy-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-(N-methylpiperazinyl)iminopiperidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-tetrahydropyranloxy)-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

20 4-amino-5-(3-bromophenyl)-7-(6-morpholinylethoxy-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-ethoxypiperidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

25 4-amino-5-(3-bromophenyl)-7-(6-(4-(2-ethoxyethoxy)piperidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-(4-tetrahydropyranloxyethyl)piperidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

30 4-amino-5-(3-bromophenyl)-7-(6-(3-(R)-tetrahydrofuranloxy)piperidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(3-(S)-tetrahydrofuroxyloxy)piperidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(trans-3-ethoxy-4-hydroxy)pyrrolidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

5 4-amino-5-(3-bromophenyl)-7-(6-(cis-3-ethoxy-4-hydroxy)pyrrolidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(trans-3-ethoxy-4-hydroxy)pyrrolidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(trans-3,4-bis-ethoxy)pyrrolidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

10 4-amino-5-(3-bromophenyl)-7-(6-(trans-3,4-bis-ethoxy)pyrrolidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(trans-3,4-bis-ethoxy)pyrrolidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(cis-3,4-bis-ethoxy)pyrrolidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

15 4-amino-5-(3-bromophenyl)-7-(6-(cis-3,4-bis-ethoxy)pyrrolidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(cis-3,4-bis-ethoxy)pyrrolidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(cis-3-amino-4-hydroxy)pyrrolidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

20 4-amino-5-(3-bromophenyl)-7-(6-(cis-3-amino-4-hydroxy)pyrrolidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(1,4-dioxa-8-azaspiro[4.5]decan-8-yl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(2-pyridyl)-7-(6-(1,4-dioxa-8-azaspiro[4.5]decan-8-yl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

25 4-amino-5-(2,3-dichlorophenyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(2-pyridyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(2-ethoxyphenyl)-7-(6-(1,4-dioxa-8-azaspiro[4.5]decan-8-yl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(2-bromo-5-ethoxyphenyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine;

30 4-amino-5-(2,3-d)pyrimidine;

4-amino-5-(2,5-dichlorophenyl)-7-(6-morpholiny-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(2,5-dimethylphenyl)-7-(6-morpholiny-3-pyridyl)pyrido[2,3-d]pyrimidine

4-amino-5-(3-fluorophenyl)-7-(6-morpholiny-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-trifluoromethylphenyl)-7-(6-morpholiny-3-pyridyl)pyrido[2,3-d]pyrimidine;

5 4-amino-5-(3-fluoro-5-trifluoromethylphenyl)-7-(6-(1,4-dioxa-8-azaspiro[4.5]decan-8-yl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3,5-dichlorophenyl)-7-(6-(1,4-dioxa-8-azaspiro[4.5]decan-8-yl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

10 4-amino-5-(3-bromophenyl)-7-(6-(1,5-dioxa-9-azaspiro[5.5]undecan-9-yl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(4-bromo-2-thienyl)-7-(6-(1,4-dioxa-8-azaspiro[4.5]decan-8-yl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-tertbutyl)piperidinyl-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

15 4-amino-5-(3-bromophenyl)-7-(6-(4-N-formyl)piperidinyl-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromo-2-thienyl)-7-(6-(4,4-ethylenedioxypiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

20 4-amino-5-(3-cyanophenyl)-7-(6-morpholiny-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-Bromophenyl)-7-(6-(S-O-ethyl-2-hydroxymethylpyrrolidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-((2S,3S)-2,3-dimethyl-1,4-dioxa-8-azaspiro[4.5]decan-8-yl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

25 4-amino-5-(3-bromophenyl)-7-(6-(4,4-(cis-1,2-dioxy-cyclopentyl)piperidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-acetyl-1-oxa-4,8-diazaspiro[4.5]decan-8-yl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-((2R,3R)-2,3-bis(methoxymethyl)-1,4-dioxa-8-azaspiro[4.5]decan-8-yl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4,4-(cis-3,4-dioxy-oxacyclopentyl)piperidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

5 4-amino-5-(3-bromophenyl)-7-(6-(3-methoxy-1,5-dioxa-9-azaspiro[5.5]undecan-9-yl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(1,5-dioxa-3-hydroxymethyl-9-azaspiro[5.5]undecan-9-yl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(1,7,14-trioxa-11-azadispiro[4.2.5.2]pentadecan-11-yl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

10 4-amino-5-(3-bromophenyl)-7-(6-(4-tetrahydropyranyl)-7-(6-morpholinyl-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(4-tetrahydropyranyl)-7-(6-morpholinyl-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-morpholinyliminopiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

15 4-amino-5-(3-bromophenyl)-7-(6-(4-(N-methylpiperazinyl)iminopiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-(1,2,4-triazol-1-yl)iminopiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-indolyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine;

20 4-amino-5-(5-indolyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-ethylpiperidinylcarboxylate)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(2-phenylmethyl-3(2H)-pyridazinone-6-yl)pyrido[2,3-d]pyrimidine;

25 4-amino-5-(3-bromophenyl)-7-(6-(4-(morpholinylcarboxamide)piperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-(N-morpholinylaminocarboxamide)piperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-(N,N-dimethylaminocarboxamide)piperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

30 4-amino-5-(3-bromophenyl)-7-(6-(4-(N,N-dimethylaminocarboxamide)piperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-(N-methyl-N-methoxyethylcarboxamide)piperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(4-quinolyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-(N-methoxyethylcarboxamide)piperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

5 4-amino-5-(2-bromophenyl)-7-(6-(1,4-dioxa-8-azaspiro[4.5]decan-8-yl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-hydroxymethylpiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(2-bromophenyl)-7-(6-(1,4-dioxa-8-azaspiro[4.5]decan-8-yl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

10 4-amino-5-(2-bromophenyl)-7-(6-(4-hydroxypiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-N-acetylpirazinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-cyanopiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

15 4-amino-5-(3-bromophenyl)-7-(6-(4-N-(4-fluorophenyl)piperazinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(4-fluorophenyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-morpholinylbenzenesulfonamide)pyrido[2,3-d]pyrimidine;

20 4-amino-5-(3-bromophenyl)-7-(4-N-1,4-dioxa-8-azaspiro[4.5]decan-8-ylbenzenesulfonamide)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-N-cyclopropylbenzenesulfonamide)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-piperidinebenzenesulfonamide)pyrido[2,3-d]pyrimidine;

25 4-amino-5-(3-bromophenyl)-7-(4-(4-cyanopiperidine)benzenesulfonamide)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-N-cyclopropylmethylbenzenesulfonamide)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-N,N-dimethylaminobenzenesulfonamide)pyrido[2,3-d]pyrimidine;

30 4-amino-5-(3-bromophenyl)-7-(4-(4-cyanopiperidine)benzenesulfonamide)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-N-(S)-2-hydroxymethylpyrrolidinebenzenesulfonamide)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(4-hydroxypiperidine)benzenesulfonamide)pyrido[2,3-d]pyrimidine;

5 4-amino-5-(3-bromophenyl)-7-(4-(cis-3,5-dimethylmorpholinyl)benzenesulfonamide)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(3-fluoro-4-thiomorpholinylphenyl)pyrido[2,3-d]pyrimidine;

10 4-amino-5-(4-fluorophenyl)-7-(6-(thiomorpholinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(4-fluorophenyl)-7-(6-(4,4-dioxothiomorpholinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-methoxy-5-(3-bromophenyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(4-dioxa-8-azaspiro[4.5]decan-8-ylcarboxamide)phenyl)pyrido[2,3-d]pyrimidine;

15 4-amino-5-(3-bromophenyl)-7-(4-(N-cyclopropylcarboxamide)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(morpholinylcarboxamide)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-N-cyclopropylamino-3-pyridyl)pyrido[2,3-d]pyrimidine;

20 4-amino-5-(3-bromophenyl)-7-(4-(4-hydroxypiperidinylcarboxamide)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(S)-hydroxymethylpyrrolidinyl-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-(2-ethoxyethoxy)piperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

25 4-amino-5-(3-bromophenyl)-7-(6-hexahydropyrimidine)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(4,4-difluorocyclohexyl)-7-(6-(1,4-dioxa-8-azaspiro[4.5]decan-8-yl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(S)-2-ethoxyethoxypyrrolidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(R)-2-ethoxyethoxypyrrolidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

5 4-amino-5-(3-bromophenyl)-7-(6-(cis-3,4-dihydroxypyrrolidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-((3aR,6aS)-2-oxo-tetrahydro-3aH-[1,3]dioxolo[4,5-c]pyrrol-5-yl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(cis-2,3-dihydroxypyrrolidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(S,R-2-hydroxymethyl-4-hydroxypyrrolidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(R-2-hydroxymethyl-4-pyrrolidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

15 4-amino-5-(3-bromophenyl)-7-(6-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptan-5-yl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(2-imidizolidone-1-yl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(1,1-dimethyl-3-butenyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine;

20 4-amino-5-(3-bromophenyl)-7-(6-(2,4-dioxo-(1H,3H)-quinazolin-3-yl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-morpholinylcarboxamide-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-morpholinylcarboxamide-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

25 4-amino-5-(3-bromophenyl)-7-(6-methoxy-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-N,N-diethoxyethylamino-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-ethoxymethylpiperidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-(4-tetrahydropyranoylmethyl)piperidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-ethoxyethoxymethyl)piperidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

5 4-amino-5-(3-bromophenyl)-7-(6-N-methyl-N-1,3-dioxolanemethylamino)-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(1,4-dioxaspiro[4.5]decanyl-8-oxy)-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-dihydroxymethylmethoxy-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

10 4-amino-5-(3-bromophenyl)-7-(6-(3-pyridyloxy)-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4,7-epoxy-7-methyl-2,3,3A,4,5,6,7,7a-octahydro-1H-isoindolyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-N-ethyl-N-methoxyethyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

15 4-amino-5-(3-bromophenyl)-7-(6-(4-N-methyl-N-methoxyethyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(3,4-dimethoxymethoxypyrrolidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

20 4-amino-5-(3-bromophenyl)-7-(6-(hexahydro-1H-furo[3,4-c]pyrrol-5-yl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(hexahydro-1H-furo[3,4-c]pyrrol-5-yl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(trans-3-hydroxy-4-methylpyrrolidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

25 4-amino-5-(3-bromophenyl)-7-(6-(trans-3-hydroxy-4-methylpyrrolidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(cis-3-hydroxy-4-methylpyrrolidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(*cis*-3-hydroxy-4-methylpyrrolidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(*trans*-3-cyano-4-hydroxylpyrrolidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

5 4-amino-5-(3-bromophenyl)-7-(6-(3-hydroxy-4-tert-butylcarboxamidepyrrolidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(S-2-(4-tetrahydropyranloxy)methylpyrrolidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(3-(4-tetrahydropyranloxy)iminopyrrolidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

10 4-amino-5-(3-bromophenyl)-7-(2-morpholiny-5-thiazoyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(5-bromo-2-thienyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(2,5-dimethyl-3-thienyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(5-chloro-2-thienyl)pyrido[2,3-d]pyrimidine;

15 4-amino-5-(3-bromophenyl)-7-(2,4-dimethyl-5-thiazoyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(5-methyl-2-thienyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(2-furanyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(2-(1,4-dioxa-8-azaspiro[4.5]decan-8-yl)-5-thiazoyl)pyrido[2,3-d]pyrimidine;

20 4-amino-5-(3-bromophenyl)-7-(3-thienyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(3-methyl-2-thienyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(2-morpholiny-4-thiazoyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(2-morpholiny-4-trifluoromethyl-5-thiazoyl)pyrido[2,3-d]pyrimidine;

25 4-amino-5-(3-bromophenyl)-7-(5-morpholiny-2-thienyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-methyl-2-morpholiny-5-thiazoyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(2,5-dichloro-3-thienyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(2,5-dimethyl-3-furanyl)pyrido[2,3-d]pyrimidine;

30 4-amino-5-(3-bromophenyl)-7-(N-methyl-2-pyrrolyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(2-N,N-dimethylamino-5-thiazoyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(2-morpholinyl-5-thiazoyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(2-(4,4-dioxythiomorpholinyl)-5-thiazoyl)pyrido[2,3-d]pyrimidine;

5 4-amino-5-(3-bromophenyl)-7-(2-(1,1-dioxidothiomorpholinyl)-5-thiazoyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(2-morpholinyl-5-oxazolyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(2-N-methyl-N-methoxyethylamino-5-thiazoyl)pyrido[2,3-d]pyrimidine;

10 4-amino-5-(3-bromophenyl)-7-(2-N-methyl-N-ethylamino-5-thiazoyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(2-N-methyl-N-propylamino-5-thiazoyl)pyrido[2,3-d]pyrimidine;

15 4-amino-5-(3-bromophenyl)-7-(2-(N-methylpiperazinyl)-5-thiazoyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(2-(N-(2-pyridyl)piperazinyl)-5-thiazoyl)pyrido[2,3-d]pyrimidine;

20 4-amino-5-(3-bromophenyl)-7-(2-N-methy-N-(2-pyridylethyl)-5-thiazoyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(2-(4-oxopiperazinyl)-5-thiazoyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(2-(4-(N-morpholinyl)iminopiperazinyl)-5-thiazoyl)pyrido[2,3-d]pyrimidine;

25 4-amino-5-(3-bromophenyl)-7-(6-N-morpholine-3-pyridinesulfonamide)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(2-(4-oxopiperidinyl)-5-pyrimidyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(2-(4,4-dioxethylenepiperidinyl)-5-pyrimidyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(5-(1,4-dioxa-8-azaspiro[4.5]decan-8-yl)-2-pyrazinyl)pyrido[2,3-d]pyrimidine;

5 4-amino-5-(3-bromophenyl)-7-(5-(4-oxopiperidinyl)-2-pyrazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-N-cyclopropyl-3-pyridinesulfonamide)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(N-1,4-dioxa-8-azaspiro[4.5]decan-8-yl)-3-pyridylsulfonamide)pyrido[2,3-d]pyrimidine;

10 4-amino-5-(3-bromophenyl)-7-(2-(4-(4-tetrahydropyranloxy)iminopiperidinyl)-5-pyrazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-(phenylmethoxy)iminopiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-(tert-butyloxy)iminopiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

15 4-amino-5-(3-bromophenyl)-7-(6-(4-(cyclohexyloxy)iminopiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-hydroxyiminopiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-(4-tetrahydropyranloxy)iminopiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

20 4-amino-5-(3-bromophenyl)-7-(6-(4-(4-methoxyethoxyiminopiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-(2-thenylmethoxy)iminopiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

25 4-amino-5-(3-bromophenyl)-7-(6-(4-(4-tetrahydropyranloxy)iminoethyl)-4-hydroxypiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-(5'H-2-oxyfuranyl)-4-hydroxypiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-(1-(4-tetrahydropyranloxy)iminoethyl)-4-hydroxypiperidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-(4'-acetyl-4'-hydroxypiperidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-(1-(isopropylcarboxymethoxy)iminoethyl))-4-hydroxypiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

5 4-amino-5-(3-bromophenyl)-7-(6-(4-(1-(ethylcarboxymethoxy)iminoethyl))-4-hydroxypiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-(1-(methylcarboxymethoxy)iminoethyl))-4-hydroxypiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-(1-(2-tetrahydropyranloxy)iminoethyl))-4-hydroxypiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

10 4-amino-5-(3-bromophenyl)-7-(6-(4-(1-(allyloxy)iminoethyl))-4-hydroxypiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-(1-(ethoxy)iminoethyl))-4-hydroxypiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

15 4-amino-5-(3-bromophenyl)-7-(6-(4-(1-(methoxy)iminoethyl))-4-hydroxypiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-(1-(hydroxy)iminoethyl))-4-hydroxypiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-(2-tetrahydropyranloxy)iminopiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

20 4-amino-5-(3-bromophenyl)-7-(6-(4-(1-(isopropylcarboxymethoxy)iminopiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-(4-(4-hydroxy-4-(1-(4-tetrahydropyranloxy)iminoethyl))-4-hydroxypiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-(3-butyrolactone)-4-hydroxypiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

25 4-amino-5-(3-bromophenyl)-7-(6-(4-(2-butyrolactone)-4-hydroxypiperidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-acetyl-4-hydroxypiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

30 4-amino-5-(3-bromophenyl)-7-(6-(4-acetyl-4-hydroxypiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(3-hydroxyazetidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-((1R,5S)-3-hydroxy-8-azabicyclo[3.2.1]octan-8-yl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

5 4-amino-5-(3-bromophenyl)-7-(6-(cis-2,3-dihydroxypiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(N-methyl-N-(3-pyridylmethyl)amino)-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(1,2,3,6-tetrahydropyridyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

10 4-amino-5-(3-bromophenyl)-7-(6-(4-(N-4'-methoxyphenylcarbamoyl)piperidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-(2-butyrolactone)-4-hydroxypiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

15 4-amino-5-(3-bromophenyl)-7-(6-(trans-3,4- bis(N-4'-methoxyphenylcarbamoyl)pyrrolidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-((1S,5R)-3-hydroxy-8-azabicyclo[3.2.1]octan-8-yl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(S,S-trans-3,4-dihydroxypyrrolidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

20 4-amino-5-(3-bromophenyl)-7-(6-(R,R-trans-3,4-dihydroxypyrrolidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(R,R-trans-3,4-dihydroxypyrrolidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(R,R-trans-3,4-dihydroxypyrrolidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

25 4-amino-5-(3-bromophenyl)-7-(6-(4-oxo-1-phenyl-1,3,8-triaspiro[4.5]decan-8-yl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(1-oxa-4-oxo-4-thia-8-azaspiro[4.5]decan-8-yl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(1-oxa-4,4-dioxido-4-thia-8-azaspiro[4.5]decan-8-yl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

30 4-amino-5-(3-bromophenyl)-7-(6-(1-oxa-4,4-dioxido-4-thia-8-azaspiro[4.5]decan-8-yl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-oxo-1-phenyl-1,3,8-triazaspiro[4.5]dec-2-en-8-yl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-(2-keto-1-benzimidazolinyl)piperidinyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

5 4-amino-5-(3-bromophenyl)-7-(6-(4-oxothiomorpholiny)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-(2-keto-1-benzimidazolinyl)piperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(N-methyl-N-(2-pyridylethyl)amino)-3-pyridyl)pyrido[2,3-d]pyrimidine;

10 4-amino-5-(3-bromophenyl)-7-(6-(N-methyl-N-(4-pyridylethyl)amino)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(N-(3-pyridylmethyl)amino-3-pyridyl)pyrido[2,3-d]pyrimidine;

15 4-amino-5-(3-bromophenyl)-7-(6-(2-hydroxymethylpiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(1-oxa-4-thia-8-azaspiro[4.5]decan-8-yl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-hydroxy-4-(4-bromophenyl)piperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

20 4-amino-5-(3-bromophenyl)-7-(6-(4-N-(2-pyridnyl)piperazinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-N-(2-hydroxyethoxyethyl)piperazinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

25 4-amino-5-(3-bromophenyl)-7-(6-(4,4-diacetoxyethylthio)piperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(N-methy-N-(3-pyridylmethyl)amino)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-pyrrolidinylpiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

30 4-amino-5-(3-bromophenyl)-7-(6-(4-pyrrolidinylpiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(2-(1H-imidazol-4-yl)ethylamino)-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-N-cyanomethylpiperazinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

5 4-amino-5-(3-bromophenyl)-7-(6-(3-hydroxypyrroldinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-methylpiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(cis-3,5-dimethylmorpholiny)-3-pyridyl)pyrido[2,3-d]pyrimidine;

10 4-amino-5-(3-bromophenyl)-7-(6-(1,1-dioxidothiomorpholiny)-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4,4-difluoropipridinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(1,1-dioxidothiazolidin-3-yl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

15 4-amino-5-(3-bromophenyl)-7-(6-thiazolidinyl-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(1,1-dioxidothiazolidin-3-yl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-thiomorpholiny-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

20 4-amino-5-(3-bromophenyl)-7-(6-(2,5-dihydropyrroly)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(1,3-dioxa-8-azaspiro[4.5]decan-8-yl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-hydroxy-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

25 4-amino-5-(2,3-dichlorophenyl)-7-(6-(1,4-dioxa-8-azaspiro[4.5]decan-8-yl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-isopropyl-7-(6-(1,4-dioxa-8-azaspiro[4.5]decan-8-yl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-piperidinyl-3-pyridyl)pyrido[2,3-d]pyrimidine;

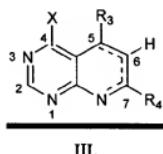
4-amino-5-(3-bromophenyl)-7-(6-(4-tetrahydropyranloxyimino)pyrrolidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine; and

4-amino-5-(2-trifluorophenylphenyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine.

5

15. A pharmaceutical composition comprising a compound according to Claim 10 and a pharmaceutically acceptable carrier.

16. A compound of formula III



wherein X is selected from the group consisting of hydroxy and halogen;

R³ is selected from the group consisting of alkenyl, alkyl, alkynyl, aryl, arylalkyl, cycloalkyl, cycloalkylalkyl, heterocycle, heterocyclealkyl, heterocyclealkylcarbonyl, (N₁Z₂)alkyl, and -R^AR^B;

15 Z₁ and Z₂ are each independently selected from the group consisting of hydrogen, alkoxy carbonyl, alkyl, alkyl carbonyl, benzyl, benzyloxy carbonyl, and formyl;

R^A is selected from the group consisting of aryl and arylalkyl;

16 R^B is selected from aryl, arylalkoxy, arylalkyl, aryloxy, heterocycle, and heterocyclealkyl;

R⁴ is selected from the group consisting of alkenyl, alkoxyalkynyl, alkyl, alkynyl, cycloalkyl, aryl, arylalkyl, heterocycle, heterocyclealkyl, and -R^CR^DR^E;

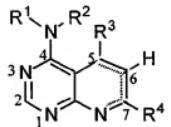
R^C is selected from the group consisting of aryl, arylalkyl, heterocycle, and heterocyclealkyl;

20 R^D is selected from the group consisting of aryl, arylalkoxy, arylalkoxyimino, arylalkyl, aryloxy, heterocycle, heterocyclealkoxy, heterocyclealkyl, heterocyclecarbonyl, heterocycleimino, heterocycleoxy, heterocycleoxyalkyl, heterocycleoxyimino, heterocycleoxyiminoalkyl, and heterocyclesulfonyl; and

5 R^E is absent or selected from aryl, arylalkoxy, arylalkoxyimino, arylalkyl, aryloxy, heterocycle, heterocyclealkoxy, heterocyclealkyl, heterocyclecarbonyl, heterocycleimino, heterocleoxy, heterocleoxyalkyl, heterocleoxyimino, heterocleoxyiminoalkyl, and heterocyclesulfonyl; and a dashed line --- indicates that a double bond is optionally present provided that proper valencies are maintained.

17. A compound according to claim 15 wherein said compound is an intermediate in a process to produce a compound according to claim 10.

10 18. A process for the preparation of an adenosine kinase inhibiting compound of formula I



I,

wherein:

15 R^1 and R^2 are hydrogen;

R^3 is selected from the group consisting of alkenyl, alkyl, alkynyl, aryl, arylalkyl, cycloalkyl, cycloalkylalkyl, heterocycle, heterocyclealkyl, heterocyclealkylcarbonyl, $(NZ_1Z_2)alkyl$, and $-R^A R^B$;

20 Z_1 and Z_2 are each independently selected from the group consisting of hydrogen, alkoxycarbonyl, alkyl, alkylcarbonyl, benzyl, benzyloxycarbonyl, and formyl;

R^A is selected from the group consisting aryl and arylalkyl;

R^B is selected from aryl, arylalkoxy, arylalkyl, aryloxy, heterocycle, and heterocyclealkyl;

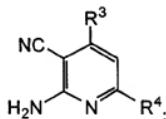
25 R^4 is selected from the group consisting of alkenyl, alkoxyalkynyl, alkyl, alkynyl, cycloalkyl, aryl, arylalkyl, heterocycle, heterocyclealkyl, and $-R^C R^D R^E$;

R^C is selected from aryl, arylalkyl, heterocycle, and heterocyclealkyl;

R^D is selected from aryl, arylalkoxy, arylalkoxyimino, arylalkyl, aryloxy, heterocycle, heterocyclealkoxy, heterocyclealkyl, heterocyclecarbonyl, heterocycleimino, heterocycloxy, heterocycloxyalkyl, heterocycloxyimino, heterocycloxyiminoalkyl, and heterocyclesulfonyl; and

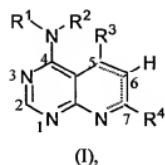
5 R^E is absent or selected from aryl, arylalkoxy, arylalkoxyimino, arylalkyl, aryloxy, heterocycle, heterocyclealkoxy, heterocyclealkyl, heterocyclecarbonyl, heterocycleimino, heterocycloxy, heterocycloxyalkyl, heterocycloxyimino, heterocycloxyiminoalkyl, and heterocyclesulfonyl; and

a dashed line --- indicates that a double bond is optionally present provided that
 10 proper valencies are maintained;
 the method comprising:
 (a) reacting a ketone having the formula $R^4\text{-CO-CH}_3$, wherein R^4 is as defined above, with an aldehyde having the formula $R^3\text{-CHO}$, wherein R^3 is as defined above and malononitrile in the presence of an ammonium salt under anhydrous conditions and
 15 isolating a first intermediate compound having the structure



(b) reacting the first intermediate compound with formamide at reflux for from about 1 to about 8 hours, and isolating the compound of formula I which has a double bond between the 5,6 carbons and a double bond between the 7 carbon and the 8 nitrogen and then,
 20
 (c) optionally reducing the compound from step (b) to form a partially reduced or fully reduced right side of formula I by catalytic hydrogenation.

19. A process for the preparation of an adenosine kinase inhibiting compound having the formula



5 wherein:

R¹ and R² are hydrogen;

R³ is selected from the group consisting of alkenyl, alkyl, alkynyl, aryl, arylalkyl, cycloalkyl, cycloalkylalkyl, heterocycle, heterocyclealkyl, heterocyclealkylcarbonyl, (NZ₁Z₂)alkyl, and -R^AR^B;

10 Z₁ and Z₂ are each independently selected from the group consisting of hydrogen, alkoxy carbonyl, alkyl, alkyl carbonyl, benzyl, benzyloxycarbonyl, and formyl;

R^A is selected from the group consisting of aryl and arylalkyl;

R^B is selected from aryl, arylalkoxy, arylalkyl, aryloxy, heterocycle, and heterocyclealkyl;

15 R⁴ is selected from the group consisting of alkenyl, alkoxyalkynyl, alkyl, alkynyl, cycloalkyl, aryl, arylalkyl, heterocycle, heterocyclealkyl, and -R^CR^DR^E;

R^C is selected from aryl, arylalkyl, heterocycle, and heterocyclealkyl;

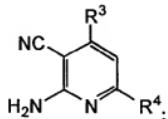
R^D is selected from aryl, arylalkoxy, arylalkoxyimino, arylalkyl, aryloxy, heterocycle, heterocyclealkoxy, heterocyclealkyl, heterocyclecarbonyl, heterocycleimino, 20 heterocycleoxy, heterocycleoxyalkyl, heterocycleoxyimino, heterocycleoxyiminoalkyl, and heterocyclesulfonyl; and

R^E is absent or selected from aryl, arylalkoxy, arylalkoxyimino, arylalkyl, aryloxy, heterocycle, heterocyclealkoxy, heterocyclealkyl, heterocyclecarbonyl, heterocycleimino, heterocycleoxy, heterocycleoxyalkyl, heterocycleoxyimino, heterocycleoxyiminoalkyl, 25 and heterocyclesulfonyl; and

a dashed line --- indicates that a double bond is optionally present provided that proper valencies are maintained;

the method comprising

(a) reacting a ketone having the formula $R^4C(O)CH_3$, wherein R^4 is as defined above, with an dicyanoalkene compound having the formula $R^3CH=C(CN)_2$, wherein R^3 is as defined above by heating at reflux and isolating a first intermediate compound having the structure



(b) reacting the first intermediate compound with formamide at reflux for from about 1 to about 8 hours, and isolating the compound of formula I which has a double bond between the 5 and 6 carbons and a double bond between the 7 carbon and the 8 nitrogen and

10 (c) optionally reducing the compound from step (b) to form a partially reduced or fully reduced right side of formula I by catalytic hydrogenation.

INTERNATIONAL SEARCH REPORT

Int. onal Application No
PCT/US 99/24901

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07D471/04 A61K31/519 A61P25/00 A61P9/00 C07D519/00
//(C07D471/04,239:00,221:00),(C07D519/00,471:00,451:00),
(C07D519/00,471:00,471:00)

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07D A61K A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	SWATI ET AL: "SYNTHESIS AND ANTIMICROBIAL EVALUATION OF SOME SUBSTITUTED PYRIDO U2,3-DPYRIMIDINES" INDIAN JOURNAL OF PHARMACEUTICAL SCIENCES, XX, XX, vol. 57, no. 6, 1 November 1995 (1995-11-01), pages 229-232, XP020271942 Bombay, India ISSN: 0250-474X table, compounds IIIa-IIIc ---	7,10,11, 15 -/-



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

* Special categories of cited documents

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority, claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

T later document published after the international filing date or priority date and not in conflict with the application but related to understand the principle or theory underlying the invention

X document of particular relevance, the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

Y document of particular relevance, the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

S document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
9 March 2000	22/03/2000
Name and mailing address of the ISA European Patent Office, P. B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Authorized officer Alfaro Faus, I

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 99/24901

C(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	SWATI ET AL: "SYNTHESIS OF SOME PYRIDOU2,3-DPYRIMIDINE DERIVATIVES AND THEIR ANTIMICROBIAL ACTIVITY" HETEROCYCLIC COMMUNICATIONS, IL, FREUND PUBLISHING HOUSE, TEL AVIV, vol. 1, no. 1, 1 January 1994 (1994-01-01), pages 89-94, XP002071943 ISSN: 0793-0283 tables 1 and 2, compounds 6a, 6b ---	7,10,11, 15
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X	DAVE C G ET AL: "DIETHYL ETHOXYMETHYLENEMALONATE IN TRIHETEROCYCLES: A NEW SYNTHESIS OF PYRIDOU3,2-EPYRIMIDOU1,2-CPYRIMIDINES" JOURNAL OF HETEROCYCLIC CHEMISTRY, 1 November 1997 (1997-11-01), XP002071947 HETEROCORPORATION. PROVO., US ISSN: 0022-152X page 1806, compounds 2a-2d ---	10-12
		-/-

INTERNATIONAL SEARCH REPORT

Inte onal Application No
PCT/US 99/24901

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	BAYOUMY B E ET AL: "NEW SYNTHESIS OF PYRIDOPYRIMIDINE AND PYRIOTETRAHYDROQUINOLINE DERIVATIVES" CHEMICAL ABSTRACTS, US, AMERICAN CHEMICAL SOCIETY, COLUMBUS, vol. 116, no. 9, 2 March 1992 (1992-03-02), page 816 XP002071948 ISSN: 0009-2258 -& DATABASE CHEMICAL ABSTRACTS 'Online! Chemical Abstracts Service, Columbus XP002132602 compounds with RNS '138744-54-4! '138744-55-5! '138744-56-6! '138744-57-7! & ZHONGHUA YAOXUE ZAZHI, vol. 43, no. 5, 1991, pages 365-71, ----	10,11,16
X	ROBINS R K ET AL: "STUDIES ON CONDENSED PYRIMIDINE SYSTEMS. XIX. A NEW SYNTHESIS OF PYRIDO[2,3-D]PYRIMIDINES. THE CONDENSATION OF 1,3-DIKETONES AND 3-KETOALDEHYDES WITH 4-AMINOPYRIMIDINES" JOURNAL OF THE AMERICAN CHEMICAL SOCIETY, US, AMERICAN CHEMICAL SOCIETY, WASHINGTON, DC, vol. 80, no. 13, 5 July 1958 (1958-07-05), pages 3449-3457, XP002071946 ISSN: 0002-7863 table V, first entry ----	16
X	WO 95 19774 A (WARNER LAMBERT CO) 27 July 1995 (1995-07-27) claims 71,74 ----	7,10,11, 15
X	WO 96 40142 A (PFIZER (US)) 19 December 1996 (1996-12-19) page 22, line 5 - line 16; claim 1 ----	7,10,15
P,X	WO 98 46605 A (ABBOTT LAB) 22 October 1998 (1998-10-22) the whole document -----	1,7,10, 15,16

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 99/24901

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. Claims Nos.: 1 to 6, 8-9
because they relate to subject matter not required to be searched by this Authority, namely:
Remark: Although claims 1 to 6, 8 and 9
are directed to a method of treatment of the human/animal
body, the search has been carried out and based on the alleged
effects of the compound/composition.
2. Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such
an extent that no meaningful International Search can be carried out, specifically:
3. Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. As all required additional search fees were timely paid by the applicant, this International Search Report covers all
searchable claims.
2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment
of any additional fee.
3. As only some of the required additional search fees were timely paid by the applicant, this International Search Report
covers only those claims for which fees were paid, specifically claims Nos.:
4. No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is
restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

The additional search fees were accompanied by the applicant's protest.

No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/US 99/24901

Patent document cited in search report	Publication date	Patent family member(s)		Publication date
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